

=> fil reg

FILE 'REGISTRY' ENTERED AT 13:50:22 ON 05 SEP 2004  
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STRUCTURE FILE UPDATES: 3 SEP 2004 HIGHEST RN 739335-06-9  
DICTIONARY FILE UPDATES: 3 SEP 2004 HIGHEST RN 739335-06-9

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

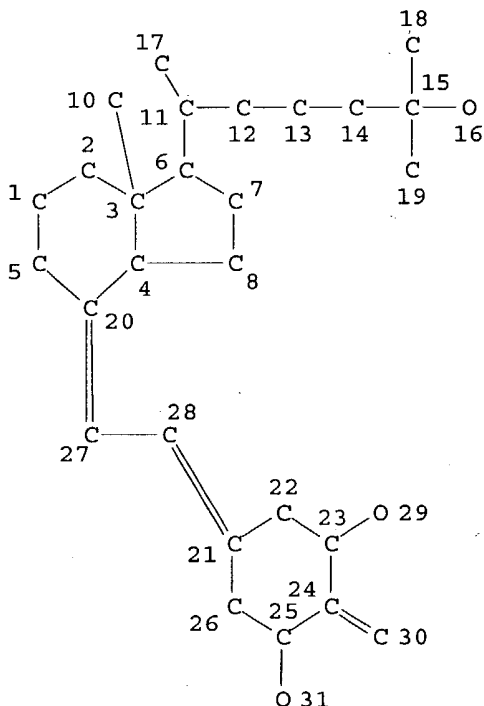
Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more  
information enter HELP PROP at an arrow prompt in the file or refer  
to the file summary sheet on the web at:  
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> d sta que l18

L16 STR



NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 30

STEREO ATTRIBUTES: NONE

L18 3 SEA FILE=REGISTRY FAM FUL L16

100.0% PROCESSED 15 ITERATIONS  
SEARCH TIME: 00.00.01

3 ANSWERS

=> d his

(FILE 'HOME' ENTERED AT 13:40:41 ON 05 SEP 2004)  
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 13:41:00 ON 05 SEP 2004

E PLUM L/AU  
L1 22 S E3,E4,E6,E7  
E CLAGETTE M/AU  
L2 1 S E2  
E CLAGETTE D/AU  
E DAME M/AU  
L3 12 S E3,E4,E6-E8  
E DELUCA H/AU  
L4 1160 S E3,E6-E10  
E DE LUCA H/AU  
L5 38 S E5,E6  
L6 1213 S L1-L5

FILE 'REGISTRY' ENTERED AT 13:42:24 ON 05 SEP 2004

FILE 'HCAPLUS' ENTERED AT 13:42:24 ON 05 SEP 2004

SET SMARTSELECT ON  
L7 SEL L6 1- RN : 2546 TERMS  
SET SMARTSELECT OFF

FILE 'REGISTRY' ENTERED AT 13:43:02 ON 05 SEP 2004

L8 2546 S L7  
L9 729 S L8 AND C6/ES AND C5-C6/ES AND 3/NR  
L10 294 S L9 AND 3/O  
L11 92 S L10 AND 27/C  
L12 54 S L11 AND 44/H  
L13 23 S L12 AND 1 3 25 TRIOL  
L14 2 S L13 AND 2 METHYLENE  
L15 52 S L12 NOT L14  
L16 STR  
L17 0 S L16 FAM SAM  
L18 3 S L16 FAM FUL  
SAV L18 QAZI782/A  
L19 3 S L14,L18

FILE 'HCAOLD' ENTERED AT 13:48:18 ON 05 SEP 2004

L20 0 S L18

FILE 'HCAPLUS' ENTERED AT 13:48:23 ON 05 SEP 2004

L21 22 S L18  
L22 19 S L21 AND L6  
L23 3 S L21 NOT L22  
L24 22 S L21-L23  
L25 0 S L24 AND LIFE(L) EXPECT?  
L26 0 S L24 AND LONGEV?  
E LONGEVITY/CT  
E E3+ALL  
L27 1 S L24 AND E3+OLD,NT,PFT,RT  
L28 22 S L24,L27

FILE 'USPATFULL, USPAT2' ENTERED AT 13:50:06 ON 05 SEP 2004

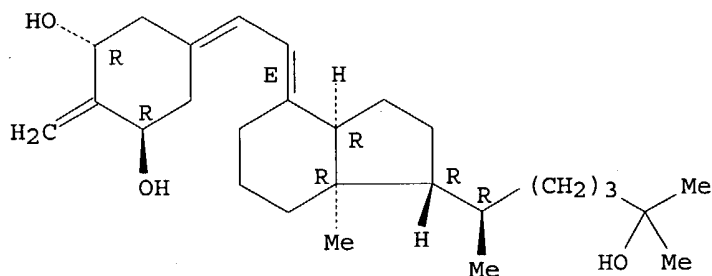
L29 24 S L18

FILE 'REGISTRY' ENTERED AT 13:50:22 ON 05 SEP 2004

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L18 ANSWER 1 OF 3 REGISTRY COPYRIGHT 2004 ACS on STN  
RN 235108-14-2 REGISTRY  
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E,14 $\beta$ )-(9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C27 H44 O3  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL  
DT.CA CAplus document type: Patent  
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES  
(Uses)

Absolute stereochemistry.  
Double bond geometry as shown.



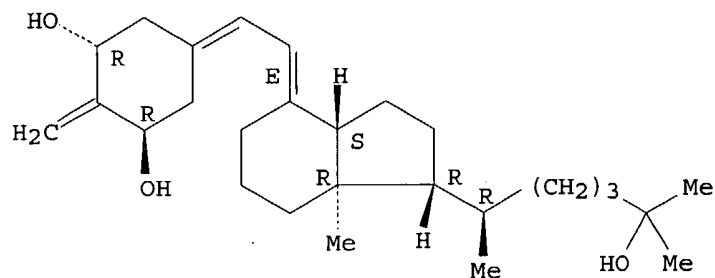
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1907 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:144749

L18 ANSWER 2 OF 3 REGISTRY COPYRIGHT 2004 ACS on STN  
RN 213319-29-0 REGISTRY  
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E)-(9CI) (CA INDEX NAME)  
OTHER NAMES:  
CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-1-[(1R)-5-hydroxy-1,5-dimethylhexyl]-7a-methyl-4H-inden-4-ylidene]ethylidene]-, (1R,3R)-  
FS STEREOSEARCH  
MF C27 H44 O3  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL  
DT.CA CAplus document type: Journal; Patent  
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); RACT (Reactant or reagent)

Absolute stereochemistry.  
Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

10 REFERENCES IN FILE CA (1907 TO DATE)

11 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:247113

REFERENCE 2: 139:271426

REFERENCE 3: 136:401925

REFERENCE 4: 136:112696

REFERENCE 5: 135:358086

REFERENCE 6: 135:304063

REFERENCE 7: 135:288953

REFERENCE 8: 133:267021

REFERENCE 9: 130:52625

REFERENCE 10: 129:245332

L18 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2004 ACS on STN

RN 213250-70-5 REGISTRY

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E,20S)- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-1-[(1S)-5-hydroxy-1,5-dimethylhexyl]-7a-methyl-4H-inden-4-ylidene]ethylidene]-, (1R,3R)-

FS STEREOSEARCH

MF C27 H44 O3

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

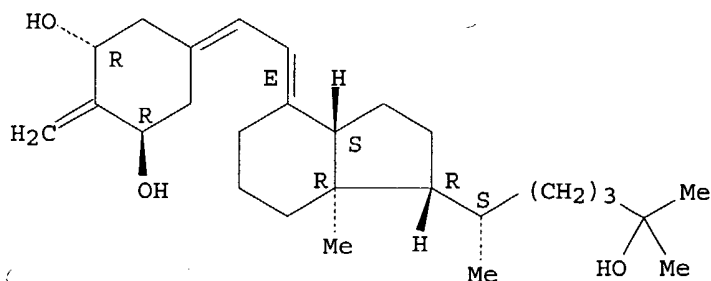
DT.CA Caplus document type: Journal; Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.

Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

15 REFERENCES IN FILE CA (1907 TO DATE)  
19 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:386155  
REFERENCE 2: 140:13126  
REFERENCE 3: 139:317525  
REFERENCE 4: 139:271459  
REFERENCE 5: 138:50247  
REFERENCE 6: 136:401925  
REFERENCE 7: 136:335278  
REFERENCE 8: 136:112696  
REFERENCE 9: 135:358086  
REFERENCE 10: 135:304063

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 13:50:36 ON 05 SEP 2004

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

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FILE COVERS 1907 - 5 Sep 2004 VOL 141 ISS 11  
FILE LAST UPDATED: 3 Sep 2004 (20040903/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=&gt; d all hitstr 127

L27 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 2002:71881 HCAPLUS  
 DN 136:112696  
 ED Entered STN: 25 Jan 2002  
 TI Use of 2-methylene-19-nor-20(S)-1 $\alpha$ ,25-dihydroxyvitamin D3 to increase bone strength and for the treatment of skin disease, cancer, and bone disease.  
 IN Deluca, Hector F.; Smith, Connie M.  
 PA Wisconsin Alumni Research Foundation, USA  
 SO PCT Int. Appl., 28 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM A61K031-59  
 CC 1-12 (Pharmacology)  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002005823	A2	20020124	WO 2001-US21706	20010710
	WO 2002005823	A3	20020523		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP	1301189	A2	20030416	EP 2001-957115	20010710
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
BR	2001012454	A	20030729	BR 2001-12454	20010710
JP	2004505022	T2	20040219	JP 2002-511755	20010710
US	2004068129	A1	20040408	US 2003-673629	20030929
PRAI	US 2000-616164	A	20000714		
	WO 2001-US21706	W	20010710		

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002005823	ICM	A61K031-59
JP 2004505022	FTERM	4C086/AA01; 4C086/AA02; 4C086/DA16; 4C086/GA16; 4C086/MA01; 4C086/MA04; 4C086/NA14; 4C086/ZA89; 4C086/ZA96; 4C086/ZA97; 4C086/ZB26
US 2004068129	ECLA	A61K007/48C4D

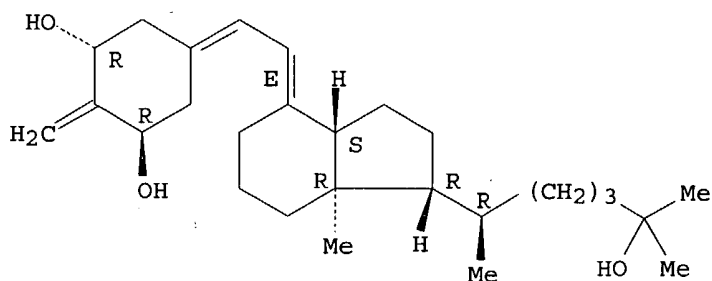
AB The invention provides pharmaceutical uses for 2-methylene-19-nor-20(S)-1 $\alpha$ ,25-dihydroxyvitamin D3. This compound is characterized by high bone calcium mobilization activity demonstrating preferential activity on bone. This results in a novel therapeutic agent for the treatment of diseases where bone formation is desired, particularly osteoporosis. This compound also exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte, thus evidencing use as an anticancer agent and for the treatment of skin diseases such as psoriasis. This compound also increases both breaking strength and crushing strength of bones evidencing use in conjunction with bone replacement surgery such as hip and knee replacements.

ST methylenenordihydroxyvitamin D3 bone strength; cancer psoriasis bone disease methylenenordihydroxyvitamin D3; skin disease osteoporosis methylenenordihydroxyvitamin D3; hip knee replacement methylenenordihydroxyvitamin D3

- IT Animal cell line  
(HL-60; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Mineral elements, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(bone; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Biological transport  
(calcium; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Intestine, neoplasm  
(colon, inhibitors; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Antitumor agents  
(colon; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Cell differentiation  
(inducers; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Antitumor agents  
(leukemia; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Osteoporosis  
(low bone turnover osteoporosis; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Antitumor agents  
(mammary gland; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Monocyte  
Osteomalacia  
Psoriasis  
(methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Vitamin D receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Bone  
(minerals; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Mammary gland  
Prostate gland  
(neoplasm, inhibitors; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Drug delivery systems  
(oral; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Bone, disease  
(osteopenia; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Drug delivery systems  
(parenterals; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Osteoporosis  
(postmenopausal; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Myelocyte  
(promyelocyte; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Antitumor agents  
(prostate gland; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)

- IT Bone, disease  
(renal osteodystrophy; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Aging, animal  
(senile osteoporosis; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Steroids, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(steroid-induced osteoporosis; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Bone  
(strength; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Osteoporosis  
(therapeutic agents; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Drug delivery systems  
(topical; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Drug delivery systems  
(transdermal; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT 32222-06-3, 1 $\alpha$ ,25-Dihydroxyvitamin D3 213319-29-0  
RL: PAC (Pharmacological activity); BIOL (Biological study)  
(methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT 213250-70-5  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT 7440-70-2, Calcium, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(transport; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT 213319-29-0  
RL: PAC (Pharmacological activity); BIOL (Biological study)  
(methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- RN 213319-29-0 HCAPLUS
- CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 $\alpha$ ,3 $\beta$ ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



- IT 213250-70-5  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(methylenenordihydroxyvitamin D3 to increase bone strength and for



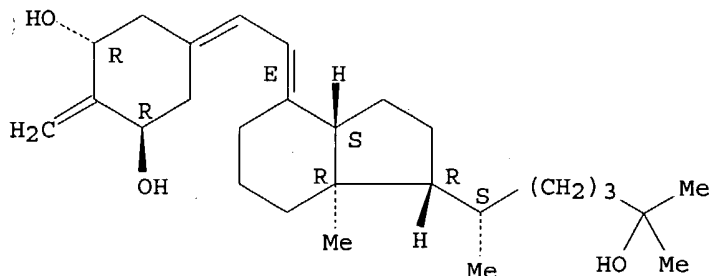
treatment of skin disease, cancer, and bone disease)

RN 213250-70-5 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E,20S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



=> s 128 not 127

L30 21 L28 NOT L27

=> d bib abs hitstr retable tot

L30 ANSWER 1 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2004:522177 HCAPLUS

TI Model of three-dimensional structure of VDR bound with Vitamin D3 analogs substituted at carbon-2

AU Sicinska, Wanda; Rotkiewicz, Piotr; DeLuca, Hector F.

CS Department of Biochemistry, University of Wisconsin-Madison, Madison, WI, 53706, USA

SO Journal of Steroid Biochemistry and Molecular Biology (2004), 89-90(1-5), 107-110

CODEN: JSBBEZ; ISSN: 0960-0760

PB : Elsevier Science Ltd.

DT Journal

LA English

AB All Vitamin D analogs possessing the A ring modified at C-2 and showing calcemic activities nest themselves in the VDR binding pocket, oriented towards Tyr 143. Such topol. resembles the position of the Vitamin D hormone in hVDRmt [Proc. Natl. Acad. Sci. U.S.A. 98 (2001) 5491]. Conversely, inactive 2 $\beta$ -methyl-19-nor-analogs anchor the receptor cavity in a distinguishably different manner, namely by their side chain. Moreover, these inactive vitamins have a different conformation around C(6)-C(7) bond. Topol. of modeled complexes suggests that a Vitamin D analog will be biol. active if its intercylic 5,7-diene moiety assumes parallel position to tryptophan aromatic rings; such orientation allows for creating  $\pi$ - $\pi$  interactions. The broad comparison of calcemic activities of the analogs, and their interactions with VDR, revealed that specific hydrophobic contacts are involved in bone calcium mobilization (BCM). These contacts occur between 21-Me group and a few amino acids (V296, L305 and L309), conserved in the nuclear receptor superfamily. In the inactive 2 $\beta$ -methyl-19-nor analogs such contacts do not exist. We speculate that two hydrophobic receptor patches, being in close contact with ligand Me groups, might influence interaction with co-modulators involved in calcium homeostasis.

IT 213250-70-5 213319-29-0

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(model of three-dimensional structure of VDR bound with Vitamin D3

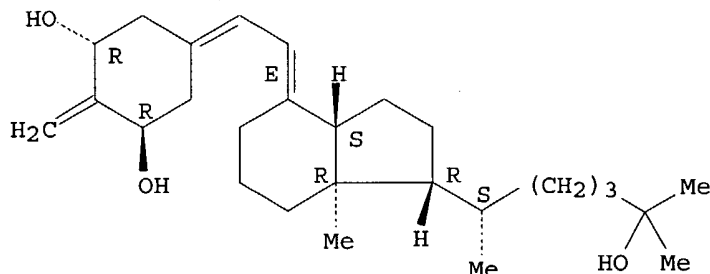
analogs substituted at carbon-2)

RN 213250-70-5 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E,20S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

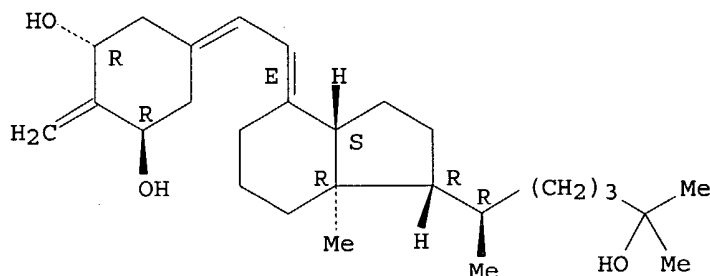


RN 213319-29-0 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



# RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
DeLuca, H	1998			US 5847173	HCAPLUS
DeLuca, H	2002			US 6440953	HCAPLUS
Maenpaa, P	2001	66	223	Steroids	HCAPLUS
Okano, T	1989	163	1444	Biochem Biophys Res	HCAPLUS
Pathrose, P	2002	17	2196	J Bone Miner Res	HCAPLUS
Rotkiewicz, P	2001	44	188	Proteins	HCAPLUS
Sicinska, W				unpublished results	
Sicinski, R	1998	41	4662	J Med Chem	HCAPLUS
Sicinski, R	2002	45	3366	J Med Chem	HCAPLUS
Tocchini-Valentini, G	2001	98	5491	Proc Natl Acad Sci U	HCAPLUS
Tripos Inc				SYBYL Modeling Progr	
Yamada, S	2003	23	89	Med Res Rev	HCAPLUS

L30 ANSWER 2 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2004:522172 HCAPLUS

TI Two-dimensional alanine scanning mutational analysis of the interaction  
between the vitamin D receptor and its ligands: studies of A-ring modified  
19-norvitamin D analogs

AU Shimizu, Masato; Yamamoto, Keiko; Mihori, Mika; Iwasaki, Yukiko; Morizono,  
Daisuke; Yamada, Sachiko

CS Institute of Biomaterial and Bioengineering, Tokyo Medical and Dental University, Tokyo, 101-0062, Japan

SO Journal of Steroid Biochemistry and Molecular Biology (2004), 89-90(1-5), 75-81  
CODEN: JSBBEZ; ISSN: 0960-0760

PB : Elsevier Science Ltd.

DT Journal

LA English

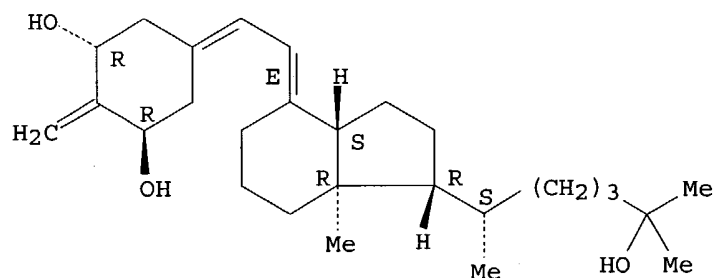
AB To clarify the structure-function relationship (SFR) of vitamin D analogs in terms of their interaction with the vitamin D receptor (VDR), we have proposed a new approach, two-dimensional alanine scanning mutational anal. (2D-ASMA). In this paper, attention was focused on the interactions around the A-ring of vitamin D. For this purpose, we synthesized four new 2-substituted 19-norvitamin D derivs. (3-6). The VDR affinity (3-6: 1, 5, 2 and 1/140, resp.) and transcriptional activity (3-6: 10, 30, 2 and 0.3, resp.) of the four compds. were evaluated relative to 1,25-(OH)2D3 (5) (normalized to 1). Then, the transcriptional activities of wild-type and 18 mutant VDRs induced by the four compds. (3-6) were investigated. The results of this 18+4 2D-ASMA were presented as a patch table, and the effects of the mutations were analyzed in comparison with the natural hormone (1) and 2-methylene-19-nor-20-epi-1,25-(OH)2D3 (2MD, 2). Of the four A-ring analogs, the 2 $\alpha$ -hydroxyethoxy derivative (3) showed striking differences in the pattern on the patch table. From the results, we suggest a docking mode of this compound (3) in which the A-ring adopts the  $\alpha$  conformation.

IT 213250-70-5  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(two-dimensional alanine scanning mutational anal. of interaction between vitamin D receptor and A-ring modified 19-norvitamin D analogs)

RN 213250-70-5 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 $\alpha$ ,3 $\beta$ ,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



## RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Choi, M	2001	9	1721	Bioorg Med Chem	HCAPLUS
Choi, M	2003	10	261	Chem Biol	HCAPLUS
DeLuca, H	1990	8	1	J Bone Miner Metab	
Evans, R	1988	240	889	Science	HCAPLUS
Mangelsdorf, D	1995	83	835	Cell	HCAPLUS
Perlman, K	1991	32	7663	Tetrahedron Lett	HCAPLUS
Pike, J	1997		105	Vitamin D	HCAPLUS
Rochel, N	2001	268	971	Eur J Biochem	HCAPLUS
Rochel, N	2000	5	173	Mol Cell	HCAPLUS
Shevde, N	2002	99	13487	Proc Natl Acad Sci U	HCAPLUS

Shimizu, M	2003	13	809	Bioorg Med Chem Lett	HCAPLUS
Sicinski, R	1998	41	4662	J Med Chem	HCAPLUS
Sicinski, R	2002	45	3366	J Med Chem	HCAPLUS
Tocchini-Valentini, G	2001	98	5491	Proc Natl Acad Sci U	HCAPLUS
Weatherman, R	1999	68	559	Annu Rev Biochem	HCAPLUS
Yamada, S	2000	6	733	Curr Pharm Des	HCAPLUS
Yamada, S	1998	41	1467	J Med Chem	HCAPLUS
Yamada, S	2003	23	89	Med Res Rev	HCAPLUS
Yamamoto, K	1995	5	979	Bioorg Med Chem Lett	HCAPLUS
Yamamoto, K	1999	9	1041	Bioorg Med Chem Lett	HCAPLUS
Yamamoto, K	1996	39	2727	J Med Chem	HCAPLUS
Yamamoto, K	1993	58	2530	J Org Chem	HCAPLUS
Yamamoto, K	2000	97	1467	Proc Natl Acad Sci U	HCAPLUS

L30 ANSWER 3 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2004:522171 HCAPLUS

TI Therapeutic potential of the 2-alkyl and 2-alkylidene-19-nor-(20S)-modified analogs of 1 $\alpha$ ,25-dihydroxyvitamin D<sub>3</sub>

AU DeLuca, Hector F.

CS Department of Biochemistry, University of Wisconsin-Madison, Madison, WI, 53706-1544, USA

SO Journal of Steroid Biochemistry and Molecular Biology (2004), 89-90(1-5), 67-73

CODEN: JSBBEZ; ISSN: 0960-0760

PB : Elsevier Science Ltd.

DT Journal

LA English

AB Five analogs of 19-nor-1 $\alpha$ ,25-dihydroxyvitamin D<sub>3</sub> are described that show highly selective and potent activities. The 2-methylene-19-nor-(20S)-1 $\alpha$ ,25-dihydroxyvitamin D<sub>3</sub> (2MD) and its 2 $\alpha$ -Me sister are selectively active on the osteoblast. 2MD is bone anabolic and causes bone formation in vivo and in vitro and is being developed as a therapy for bone loss diseases such as osteoporosis. 2-Methylene-19-nor-(20S)-bishomo-1 $\alpha$ -hydroxypregnacalciferol (2BMP) has no activity on calcium in vivo while totally suppressing circulating parathyroid hormone. Its homologs, i.e. 2-methylene-19-nor-1 $\alpha$ -hydroxy-homopregnacalciferol (2MP) and 2-methylene-19-nor-1 $\alpha$ -hydroxypregnacalciferol (2MPC) act similarly but are either less selective (2MP) or not as potent (2MPC). These abbreviated side chain analogs will be developed for diseases where a rise in serum calcium is not desired, as for example, cancer, renal osteodystrophy, psoriasis and autoimmune diseases.

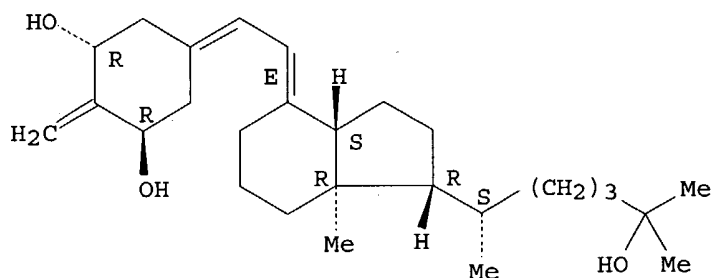
IT 213250-70-5

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(effects of 2-alkyl and 2-alkylidene-19-nor-(20S)-modified analogs of 1 $\alpha$ ,25-(OH)<sub>2</sub>D<sub>3</sub> on PTH activity/bone mineral mobilization, and their therapeutic potential for diseases where a rise in serum calcium is not desired)

RN 213250-70-5 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 $\alpha$ ,3 $\beta$ ,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



## RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Abe, J	1990	36	21	J Nutr Sci Vitaminol	HCAPLUS
Binderup, L	1992	3	401	Rev Contemp Pharmaco	
Brown, A	1997		995	Vitamin D	HCAPLUS
Calverley, M	1987	43	4609	Tetrahedron	HCAPLUS
DeLuca, H	1997		3	Vitamin D	HCAPLUS
Jones, G	1998	78	1193	Physiol Rev	HCAPLUS
Jones, G	1997		973	Vitamin D	HCAPLUS
Kobayashi, T	1994	115	373	J Biochem	HCAPLUS
Maung, H	2001	37	532	Am J Kidney Dis	HCAPLUS
Morimoto, S	1989	19	1143	Biochem Int	HCAPLUS
Perlman, K	1990	31	1823	Tetrahedron Lett	HCAPLUS
Plum, L	2002			2-Methylelene-19-nor-	
Shevde, N	2002	99	13487	Proc Natl Acad Sci U	HCAPLUS
Sicinski, R	1998	41	4662	J Med Chem	HCAPLUS
Sicinski, R	2002	45	3366	J Med Chem	HCAPLUS
Slatopolsky, E	1994	5	888	J Am Soc Nephrol	
Slatopolsky, E	2003	85	83	Kidney Int Suppl	
Stabert, B	1989	69	147	Acta Derm Venereol (	
Suda, T	2003	88	259	J Cell Biochem	HCAPLUS
Suda, T	1997		329	Vitamin D	HCAPLUS
Yamamoto, H	2003	278	31756	J Biol Chem	HCAPLUS

L30 ANSWER 4 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2004:522161 HCAPLUS

TI 2-Methylene analogs of 1 $\alpha$ -hydroxy-19-norvitamin D<sub>3</sub>: synthesis, biological activities and docking to the ligand binding domain of the rat vitamin D receptor

AU Grzywacz, Pawel; Plum, Lori A.; Sicinska, Wanda; Sicinski, Rafal R.; Prahl, Jean M.; DeLuca, Hector F.

CS Department of Biochemistry, University of Wisconsin-Madison, Madison, WI, 53706, USA

SO Journal of Steroid Biochemistry and Molecular Biology (2004), 89-90(1-5), 13-17

CODEN: JSBBEZ; ISSN: 0960-0760

PB : Elsevier Science Ltd.

DT Journal

LA English

AB In continuing efforts towards the synthesis of biol. active vitamin D compds. of potential therapeutic value, new 2-methylene-1 $\alpha$ -hydroxy-19-norvitamin D<sub>3</sub> analogs 3 and 4 with modified alkyl side chains have been synthesized. The key synthetic step involved Lythgoe-type Wittig-Horner coupling of Windaus-Grundmann type ketones 9, possessing different 17 $\beta$ -alkyl substituents, with the phosphine oxide 10 prepared from (-)-quinic acid. The prepared vitamins 3 and 4 were .apprx.eight times less potent than 1 $\alpha$ ,25-dihydroxyvitamin D<sub>3</sub> (1 $\alpha$ ,25-(OH)<sub>2</sub>D<sub>3</sub>) (1) in binding to the rat intestinal vitamin D receptor (VDR). In comparison

with the hormone 1 they exhibited slightly lower cellular HL-60 differentiation activity. When tested in vivo; the analog 3 was characterized by very high bone calcium mobilizing potency and intestinal calcium transport activity. Unexpectedly, the 25-Me compound 4 showed marked calcemic activity in both assays. Computational docking of the vitamin 3 into the binding pocket of the rat vitamin D receptor is also reported.

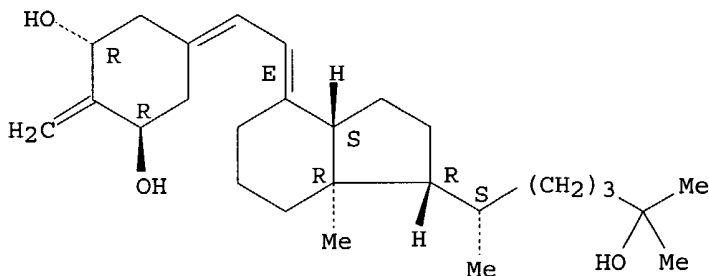
IT 213250-70-5P

RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(synthesis, biol. activities of 2-Methylene analogs of  
1 $\alpha$ -hydroxy-19-norvitamin D3 and their docking to ligand binding  
domain of rat vitamin D receptor)

RN 213250-70-5 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E,20S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



# RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Dame, M	1986	25	4523	Biochemistry	HCAPLUS
DeLuca, H	1991	3	1129	Comprehensive Medici	
DeLuca, H	1988	2	224	FASEB J	HCAPLUS
Jones, G	1998	78	1193	Physiol Rev	HCAPLUS
Norman, A	1994			Vitamin D, a pluripo	
Ostrem, V	1987	262	14164	J Biol Chem	HCAPLUS
Posner, G	1995	38	4529	J Med Chem	HCAPLUS
Rochel, N	2000	5	173	Mol Cell	HCAPLUS
Rotkiewicz, P	2001	44	188	Proteins	HCAPLUS
Shevde, N	2002	99	13487	Proc Natl Acad Sci U	HCAPLUS
Sicinski, R	1998	41	4662	J Med Chem	HCAPLUS
Suda, T	1990	10	195	Annu Rev Nutr	HCAPLUS

L30 ANSWER 5 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2004:220021 HCAPLUS

DN 140:247113

TI Method of extending the dose range of vitamin D compounds

IN Deluca, Hector F.; Pike, John W.; Shevde, Nirupama; Plum,  
Lori A.; Clagett-Dame, Margaret

PA USA

SO U.S. Pat. Appl. Publ., 17 pp.

CODEN: USXXCO

DT Patent

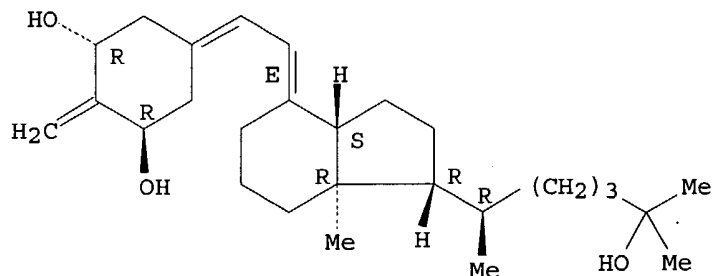
LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----

PI US 2004053813 A1 20040318 US 2002-235244 20020905  
 WO 2004022068 A1 20040318 WO 2003-US20517 20030626  
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,  
 PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,  
 UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,  
 TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,  
 CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,  
 NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,  
 GW, ML, MR, NE, SN, TD, TG  
 PRAI US 2002-235244 A 20020905  
 OS MARPAT 140:247113  
 AB Inhibitors of bone calcium resorption are administered to allow high doses  
 of vitamin D compds. or mimetics (Markush structures are given) to be  
 given with the intent of treating non-calcium related diseases such as  
 cancer, psoriasis, and autoimmune disease without the dangers of  
 calcification of kidney, heart, and aorta. Inhibitors of bone calcium  
 resorption include the bis-phosphonates, OPG or the soluble RANKL receptor  
 known as sRANK, and function to block the availability of calcium from  
 bone thereby preventing hypercalcemia and the resulting calcification of  
 soft tissues. Thus, high doses of  $1\alpha,25$ -dihydroxyvitamin D 3  
 ( $1,25$ -(OH)  $2$  D 3 ), its analogs, prodrugs, or mimetics can be utilized  
 with minimal risk to a patient. Specifically, alendronate is shown to  
 block the bone calcium mobilization activity of both  $1,25$ -(OH)  $2$  D 3 and  
 its very potent analog, 2-methylene- $19$ -nor- $20$ (S)- $1\alpha,25$ -  
 dihydroxyvitamin D 3 .  
 IT 213319-29-0  
 RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological  
 activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (method of extending dose range of vitamin D compds.)  
 RN 213319-29-0 HCAPLUS  
 CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
 ( $1\alpha,3\beta,7E$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



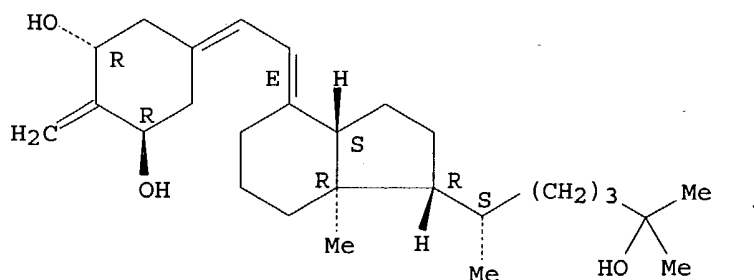
L30 ANSWER 6 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 2004:191311 HCAPLUS  
 DN 140:386155  
 TI Molecular structure of rat vitamin D receptor ligand binding domain  
 complexed with 2-carbon-substituted vitamin D3 hormone analogs and a  
 LXXLL-containing coactivator peptide  
 AU Vanhooke, Janeen L.; Benning, Matthew M.; Bauer, Cary B.; Pike, J. Wesley;  
 DeLuca, Hector F.  
 CS Department of Biochemistry, University of Wisconsin, Madison, WI, 53706,  
 USA

SO Biochemistry (2004), 43(14), 4101-4110  
 CODEN: BICHAW; ISSN: 0006-2960  
 PB American Chemical Society  
 DT Journal  
 LA English  
 AB The authors have determined the crystal structures of the ligand binding domain (LBD) of the rat vitamin D receptor in ternary complexes with a synthetic LXXLL-containing peptide and the following four ligands: 1 $\alpha$ ,25-dihydroxyvitamin D<sub>3</sub>; 2-methylene-19-nor-(20S)-1 $\alpha$ ,25-dihydroxyvitamin D<sub>3</sub> (2MD); 1 $\alpha$ -hydroxy-2-methylene-19-nor-(20S)-bishomopregnacalciferol (2Mbisp), and 2 $\alpha$ -methyl-19-nor-1 $\alpha$ ,25-dihydroxyvitamin D<sub>3</sub> (2AM20R). The conformation of the LBD is identical in each complex. Binding of the 2-carbon-modified analogs does not change the positions of the amino acids in the ligand binding site and has no effect on the interactions in the coactivator binding pocket. The CD ring of the superpotent analog, 2MD, is tilted within the binding site relative to the other ligands in this study and to (20S)-1 $\alpha$ ,25-dihydroxyvitamin D<sub>3</sub>. The aliphatic side chain of 2MD follows a different path within the binding site; nevertheless, the 25-hydroxyl group at the end of the chain occupies the same position as that of the natural ligand, and the hydrogen bonds with histidines 301 and 393 are maintained. 2Mbisp binds to the receptor despite the absence of the 25-hydroxyl group. A water mol. is observed between His 301 and His 393 in this structure, and it preserves the orientation of the histidines in the binding site. Although the  $\alpha$ -chair conformer is highly favored in solution for the A ring of 2AM20R, the crystal structures demonstrate that this ring assumes the  $\beta$ -chair conformation in all cases, and the 1 $\alpha$ -hydroxyl group is equatorial. The peptide folds as a helix and is anchored through hydrogen bonds to a surface groove formed by helices 3, 4, and 12. Electrostatic and hydrophobic interactions between the peptide and the LBD stabilize the active receptor conformation. This stabilization appears necessary for crystal growth.

IT 213250-70-5  
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
 (mol. structure of rat vitamin D receptor ligand binding domain complexed with 2-carbon-substituted vitamin D<sub>3</sub> hormone analogs and LXXLL-containing coactivator peptide)

RN 213250-70-5 HCAPLUS  
 CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 $\alpha$ ,3 $\beta$ ,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



## RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Abe, E	1981	78	4990	Proc Natl Acad Sci U	HCAPLUS
Binderup, L	1991	42	1569	Biochem Pharmacol	HCAPLUS



Bortman, P	2002	35	1	Braz J Med Biol Res	HCAPLUS
Bouillon, R	1995	16	200	Endocr Rev	HCAPLUS
Bourguet, W	1995	375	377	Nature	HCAPLUS
Chothia, C	1975	254	304	Nature	HCAPLUS
Collaborative Computati	1994	50	760	Acta Crystallogr, Se	
Dame, M	1985	82	7825	Proc Natl Acad Sci U	HCAPLUS
Darimont, B	1998	12	3343	Genes Dev	HCAPLUS
Delano, W	2002			The PyMOL molecular	
Drezner, M	1997		733	Vitamin D	HCAPLUS
Durand, B	1994	13	5370	EMBO J	HCAPLUS
Fraser, D	1973	289	817	N Engl J Med	MEDLINE
Glorieux, F	1980	303	1023	N Engl J Med	MEDLINE
Hayes, C	2000	59	531	Proc Nutr Soc	HCAPLUS
Henttu, P	1997	17	1832	Mol Cell Biol	HCAPLUS
Hosomi, J	1983	113	1950	Endocrinology	HCAPLUS
Ikekawa, N	1987	7	333	Med Res Rev	HCAPLUS
Jones, G	1998	78	1193	Physiol Rev	HCAPLUS
Kabsch, W	1976	32	922	Acta Crystallogr, Se	
Kimmel-Jehan, C	1997	341	75	Arch Biochem Biophys	HCAPLUS
Konety, B	2002	29	95	Urol Clin North Am	
Lamberg-Allardt, C	1991	49	546	Calcif Tissue Int	
Langner, A	1993	128	566	Br J Dermatol	MEDLINE
Laskowski, R	1993	26	283	J Appl Crystallogr	HCAPLUS
Lee, B	1971	55	379	J Mol Biol	HCAPLUS
Lemire, J	1992	49	26	J Cell Biochem	HCAPLUS
Macdonald, P	1991	266	18808	J Biol Chem	HCAPLUS
Massry, S	1979	242	1875	JAMA	MEDLINE
Masuyama, H	1997	11	1507	Mol Endocrinol	HCAPLUS
Murshudov, G	1997	53	240	Acta Crystallogr, Se	
Nishii, Y	2001	66	137	Steroids	HCAPLUS
Nolte, R	1998	395	137	Nature	HCAPLUS
Okamura, W	1974	71	4194	Proc Natl Acad Sci U	HCAPLUS
Osborn, J	1995	1	195	Urol Oncol	
Rachez, C	2000	246	9	Gene	HCAPLUS
Rachez, C	2000	20	2718	Mol Cell Biol	HCAPLUS
Renaud, J	1995	378	681	Nature	HCAPLUS
Rochel, N	2000	5	173	Mol Cell	HCAPLUS
Ross, T	1991	88	6555	Proc Natl Acad Sci U	HCAPLUS
Roussel, A	1991		86	Silicone Graphics Ge	
Shevde, N	2002	99	13487	Proc Natl Acad Sci U	HCAPLUS
Sicinski, R	1998	41	4662	J Med Chem	HCAPLUS
Sicinski, R	2002	45	3366	J Med Chem	HCAPLUS
Slatopolski, E	1997		849	Vitamin D	
Smith, E	1986	86	709	J Invest Dermatol	HCAPLUS
Tanaka, H	1982	204	713	Biochem J	HCAPLUS
Tocchini-Valentini, G	2001	98	5491	Proc Natl Acad Sci U	HCAPLUS
Vagin, A	1997	30	1022	J Appl Crystallogr	HCAPLUS
Wing, R	1975	97	4980	J Am Chem Soc	HCAPLUS

L30 ANSWER 7 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:796501 HCAPLUS

DN 139:271459

TI Use of carbon-2-modified-vitamin D analogs to induce the formation of new bone

IN Deluca, Hector F.; Pike, J. Wesley; Shevde, Nirupama K.

PA Wisconsin Alumni Research Foundation, USA

SO PCT Int. Appl., 48 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 2003082300 A1 20031009 WO 2003-US7443 20030312  
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,  
 PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,  
 UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,  
 CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,  
 NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,  
 GW, ML, MR, NE, SN, TD, TG

US 2003195175 A1 20031016 US 2002-105826 20020325

PRAI US 2002-105826 A 20020325

OS MARPAT 139:271459

AB It has been discovered that the 2-carbon-modified derivs. of  
 1 $\alpha$ ,25-dihydroxyvitamin D<sub>3</sub> specifically stimulate osteoblasts to form  
 new bone. The ability of the 2-carbon-modified vitamin D analogs to  
 stimulate new bone formation suggest that these compds. can be used where  
 synthesis of new bone is required. Thus, these compds. can be used either  
 systemically or locally to stimulate the growth of bone transplants, to  
 increase the rate of fracture healing and thereby reduce the time required  
 for the healing of fractures, the stimulation of bone growth when required  
 for replacement surgery, and also for the growth of bone to implants or  
 other devices required to maintain the skeleton or teeth in the proper  
 positions.

IT 213250-70-5

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)

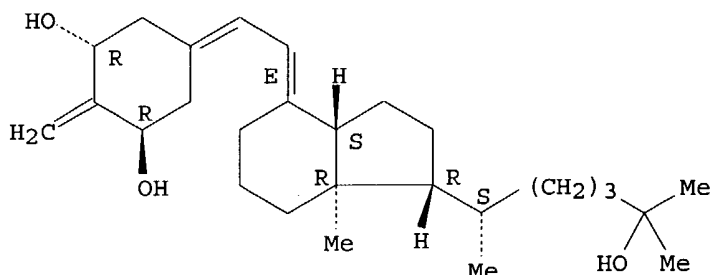
(use of carbon-2-modified-vitamin D analogs to induce the formation of  
 new bone)

RN 213250-70-5 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
 (1 $\alpha$ ,3 $\beta$ ,7E,20S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

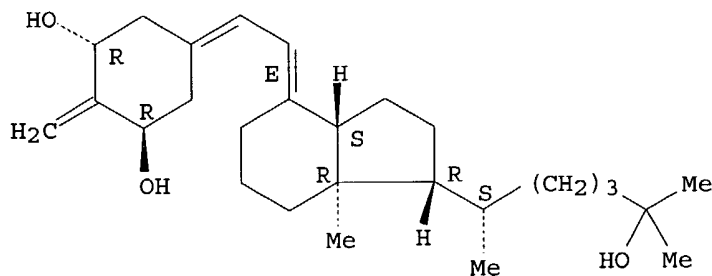


#### RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Schnoes, H	1997			WO 9711053 A	HCAPLUS
Shevde, N	2002	99	13487	PROCEEDINGS OF THE N	HCAPLUS
Sicinski	1998	41	4662	JOURNAL OF MEDICINAL	HCAPLUS
Wisconsin Alumni Res Fo	1998			WO 9841500 A	HCAPLUS
Wisconsin Alumni Res Fo	1998			WO 9841501 A	HCAPLUS
Wisconsin Alumni Res Fo	2001			WO 0174766 A	HCAPLUS
Wisconsin Alumni Res Fo	2002			WO 0205823 A	HCAPLUS
Wisconsin Alumni Res Fo	2002			WO 0205824 A	

AN 2003:680362 HCAPLUS  
 DN 140:13126  
 TI Vitamin D analogs and calcium metabolism. Bone-selective analogs  
 AU Okano, Toshio  
 CS Department of Hygienic Sciences, Kobe Pharmaceutical University, Japan  
 SO Clinical Calcium (2003), 13(7), 911-914  
 CODEN: CLCCEJ; ISSN: 0917-5857  
 PB Iyaku Janarusha  
 DT Journal; General Review  
 LA Japanese  
 AB A review. 2MD [2-methylene-19-nor-(20S)-1 $\alpha$ ,25(OH)2D3] is a bone-selective vitamin D analog that has been developed on the basis of structure-function study. The bone-selective action of the analog has been tested and confirmed both in vitro and in vivo and its clin. application as a medication for bone diseases is anticipated although its adverse effects remain unclear.  
 IT 213250-70-5  
 RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (clin. applications of bone-selective vitamin D analogs and relationship to calcium metabolism)  
 RN 213250-70-5 HCAPLUS  
 CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 $\alpha$ ,3 $\beta$ ,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



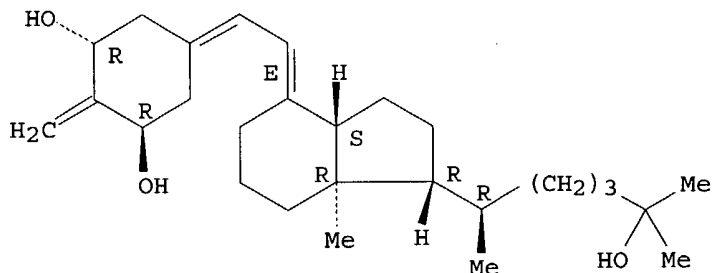
L30 ANSWER 9 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 2003:647469 HCAPLUS  
 DN 139:271426  
 TI 2-Methylene-19-nor-(20S)-1,25-dihydroxyvitamin D3 potently stimulates gene-specific DNA binding of vitamin D receptor in osteoblasts  
 AU Yamamoto, Hironori; Shevde, Nirupama K.; Warriar, Anjali; Plum, Lori A.; DeLuca, Hector F.; Pike, J. Wesley  
 CS Department of Biochemistry, University of Wisconsin-Madison, Madison, WI, 53706, USA  
 SO Journal of Biological Chemistry (2003), 278(34), 31756-31765  
 CODEN: JBCHA3; ISSN: 0021-9258  
 PB American Society for Biochemistry and Molecular Biology  
 DT Journal  
 LA English  
 AB 2-Methylene-19-nor-(20S)-1,25-dihydroxyvitamin D3 (2MD) is a highly potent analog of 1,25-dihydroxyvitamin D3 (1,25(OH)2D3) whose actions are mediated through the vitamin D receptor (VDR). The authors have replicated this increased potency of 2MD in vitro using osteoblastic cells and explored its underlying mol. mechanism. 2MD stimulates the expression of several vitamin D-sensitive genes including 25-hydroxyvitamin D3-24 hydroxylase (Cyp24), osteopontin and receptor activator of NF $\kappa$ B

IT 213319-29-0

RN 213319-29-0 HCAPLUS

19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



RETABLE	Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
=====	=====	+	+	+	=====	=====
Allan, G		1992	267	19513	J Biol Chem	HCAPLUS
Beckman, M		1998	35	1	Prog Med Chem	HCAPLUS
Beekman, J		1993	7	1266	Mol Endocrinol	HCAPLUS
Bikle, D		1992	13	765	Endocr Rev	HCAPLUS
Binderup, L		1997		1027	Vitamin D	HCAPLUS
Brown, A		1997		1027	Vitamin D	
Carlberg, C		2003	88	274	J Cell Biochem	HCAPLUS
Chang, C		1999	19	8226	Mol Cell Biol	HCAPLUS
Cheskis, B		1996	12	3309	Biochemistry	
Cook, N		1984	10	294	Endocr Rev	
Dwivedi, P		2002	277	29643	J Biol Chem	HCAPLUS
Haussler, M		1998	13	325	J Bone Miner Res	HCAPLUS
Heery, D		1997	387	733	Nature	HCAPLUS
Herdick, M		2000	57	1206	Mol Pharmacol	HCAPLUS
Hofbauer, L		2000	15	2	J Bone Miner Res	HCAPLUS
Hughes, M		1988	242	1702	Science	HCAPLUS
James, A		2002	16	2692	Mol Endocrinol	HCAPLUS

Jin, C	1996	10	945	Mol Endocrinol	HCAPLUS
Jones, G	1998	78	1193	Physiol Rev	HCAPLUS
Kissmeyer, A	1991	41	1601	Biochem Pharmacol	HCAPLUS
Kittaka, A	2003	51	357	Chem Pharm Bull (Tok	HCAPLUS
Kraichely, D	1999	274	14352	J Biol Chem	HCAPLUS
Kubodera, N	2003	88	286	J Cell Biochem	HCAPLUS
Li, Y	1997	94	9831	Proc Natl Acad Sci U	HCAPLUS
Liu, Y	2000	14	1776	Mol Endocrinol	HCAPLUS
Mackey, S	1996	10	298	Mol Endocrinol	HCAPLUS
Masuyama, H	1998	71	429	J Cell Biochem	HCAPLUS
McKenna, N	1999	20	321	Endocr Rev	HCAPLUS
Morony, S	1999	14	1478	J Bone Miner Res	HCAPLUS
Nawaz, Z	1999	96	1858	Proc Natl Acad Sci U	HCAPLUS
Norman, A	1995	22	S218	J Cell Biochem	
Ozono, K	1990	265	21881	J Biol Chem	HCAPLUS
Pathrose, P	2002	17	2196	J Bone Miner Res	HCAPLUS
Peleg, S	1995	270	10551	J Biol Chem	HCAPLUS
Pike, A	2000	28	396	Biochem Soc Trans	HCAPLUS
Pike, J	2002	9	168	Adv Ren Replace Ther	
Pike, J	1983	258	1289	J Biol Chem	HCAPLUS
Pike, J	1983	258	8554	J Biol Chem	HCAPLUS
Rochel, N	2000	5	173	Mol Cell	HCAPLUS
Rowan, B	2000	275	4475	J Biol Chem	HCAPLUS
Shang, Y	2000	103	843	Cell	HCAPLUS
Shevde, N	2000	97	7829	Proc Natl Acad Sci U	HCAPLUS
Shevde, N	2002	99	13487	Proc Natl Acad Sci U	HCAPLUS
Shiau, A	1998	95	927	Cell	HCAPLUS
Sicinski, R	1998	41	4662	J Med Chem	HCAPLUS
Sone, T	1991	266	23296	J Biol Chem	HCAPLUS
Thompson, P	2001	27	211	J Mol Endocrinol	HCAPLUS
Tocchini-Valentini, G	2001	98	5491	Proc Natl Acad Sci U	HCAPLUS
Vaisanen, S	1999	261	706	Eur J Biochem	HCAPLUS
Weinman, A	2002	26	37	Methods	
Yang, W	1999	274	16838	J Biol Chem	HCAPLUS
Zou, A	1997	272	19027	J Biol Chem	HCAPLUS

L30 ANSWER 10 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:249861 HCAPLUS

DN 139:317525

TI Interaction between vitamin D receptor and vitamin D ligands  
two-dimensional alanine scanning mutational analysis

AU Choi, Mihwa; Yamamoto, Keiko; Itoh, Toshimasa; Makishima, Makoto;  
Mangelsdorf, David J.; Moras, Dino; DeLuca, Hector F.; Yamada,  
Sachiko

CS Institute of Biomaterials and Bioengineering, Tokyo Medical and Dental  
University, Chiyoda-ku, Tokyo, 101-0062, Japan

SO Chemistry & Biology (2003), 10(3), 261-270  
CODEN: CBOLE2; ISSN: 1074-5521

PB Cell Press

DT Journal

LA English

AB We present a new method to investigate the details of interaction between  
vitamin D nuclear receptor (VDR) and various ligands, namely a  
two-dimensional alanine scanning mutational anal. In this method, the  
transactivation of various ligands is studied in conjunction with a series  
of alanine scanning mutations of the residues lining the ligand binding  
pocket (LBP) of VDR, and the complete set of results is profiled in a  
patch table. We investigated examples from four structurally diverse  
groups of known VDR ligands: the native vitamin D hormone and two compds.  
with the same side chain configuration; four 20-epi compds.; three 19-nor  
compds.; and two nonsecosteroids. The patch table of the results  
indicates characteristics of each group in terms of its interaction with  
18 LBP residues. We demonstrate the validity of this approach by

application to docking studies of the two nonsecosteroids.

IT 213250-70-5

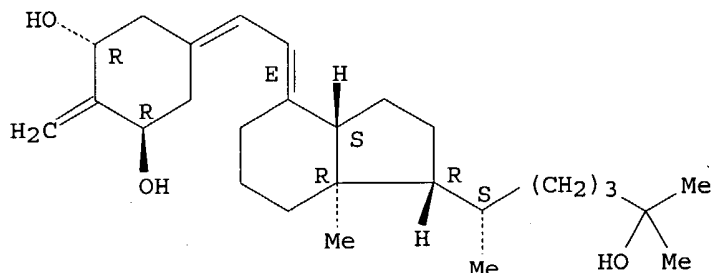
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(two-dimensional alanine scanning mutational anal. and modeling of the  
interaction between vitamin D receptor (VDR) its ligands)

RN 213250-70-5 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E,20S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

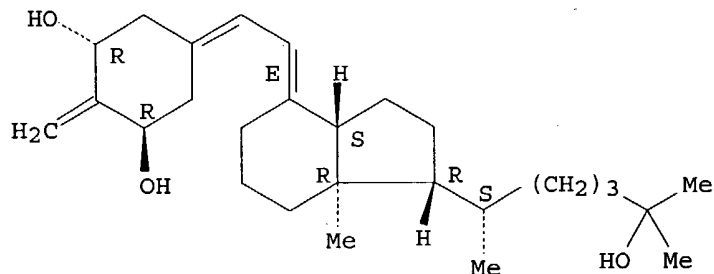


# RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Binderup, L	1991	42	1569	Biochem Pharmacol	HCAPLUS
Choi, M	2001	9	1721	Bioorg Med Chem	HCAPLUS
DeLuca, H	1990	8	1	J Bone Miner Metab	
Evans, R	1988	240	889	Science	HCAPLUS
Geller, D	2000	289	119	Science	HCAPLUS
Kobayashi, T	1993	3	1815	Bioorg Med Chem Lett	HCAPLUS
Kragballe, K	1997		1213	Vitamin D	HCAPLUS
Kramer, B	1999	37	228	Proteins	HCAPLUS
Makishima, M	2002	296	1313	Science	HCAPLUS
Mangelsdorf, D	1995	83	835	Cell	HCAPLUS
Murayama, E	1986	34	4410	Chem Pharm Bull (Tok	HCAPLUS
Narisawa, T	1974	53	1093	J Natl Cancer Inst	HCAPLUS
Noda, M	1990	87	9995	Proc Natl Acad Sci U	HCAPLUS
Pike, J	1983	258	1289	J Biol Chem	HCAPLUS
Rarey, M	1996	261	470	J Mol Biol	HCAPLUS
Rochel, N	2001	268	971	Eur J Biochem	HCAPLUS
Rochel, N	2000	5	173	Mol Cell	HCAPLUS
Shevde, N	2002	99	13487	Proc Natl Acad Sci U	HCAPLUS
Sicinski, R	2002			US 6440953	HCAPLUS
Sicinski, R	1998	41	4662	J Med Chem	HCAPLUS
Tocchini-Valentini, G	2001	98	5491	Proc Natl Acad Sci U	HCAPLUS
Umesono, K	1991	65	1255	Cell	HCAPLUS
Watkins, R	2001	292	2329	Science	HCAPLUS
Wurtz, J	1996	3	87	Nat Struct Biol	HCAPLUS
Yamada, S	1998			WO 9839292	HCAPLUS
Yamada, S	2000	6	733	Curr Pharm Des	HCAPLUS
Yamada, S	1998	41	1467	J Med Chem	HCAPLUS
Yamamoto, K	1995	5	979	Bioorg Med Chem Lett	HCAPLUS
Yamamoto, K	1999	9	1041	Bioorg Med Chem Lett	HCAPLUS
Yamamoto, K	1996	39	2727	J Med Chem	HCAPLUS
Yamamoto, K	1993	58	2530	J Org Chem	HCAPLUS
Yamamoto, K	2000	97	1467	Proc Natl Acad Sci U	HCAPLUS

DN 138:50247  
 TI A potent analog of  $1\alpha,25$ -dihydroxyvitamin D3 selectively induces bone formation  
 AU Shevde, Nirupama K.; Plum, Lori A.; Clagett-Dame, Margaret; Yamamoto, Hironori; Pike, J. Wesley; DeLuca, Hector F.  
 CS Department of Biochemistry, University of Wisconsin, Madison, WI, 53706, USA  
 SO Proceedings of the National Academy of Sciences of the United States of America (2002), 99(21), 13487-13491  
 CODEN: PNASA6; ISSN: 0027-8424  
 PB National Academy of Sciences  
 DT Journal  
 LA English  
 AB  $1,25$ -Dihydroxyvitamin D3 [ $1,25(\text{OH})_2\text{D}_3$ ] is a principal regulator of calcium and phosphorus homeostasis through actions on intestine, kidney, and bone.  $1,25(\text{OH})_2\text{D}_3$  is not considered to play a significant role in bone formation, except for its role in supporting mineralization. The authors report on the properties of 2-methylene-19-nor-( $20\text{S}$ )- $1\alpha,25(\text{OH})_2\text{D}_3$  (2MD), a highly potent analog of  $1,25(\text{OH})_2\text{D}_3$  that induces bone formation both in vitro and in vivo. Selectivity for bone was first demonstrated through the observation that 2MD is at least 30-fold more effective than  $1,25(\text{OH})_2\text{D}_3$  in stimulating osteoblast-mediated bone calcium mobilization while being only slightly more potent in supporting intestinal calcium transport. 2MD is also highly potent in promoting osteoblast-mediated osteoclast formation in vitro, a process essential to both bone resorption and formation. Most significantly, 2MD at concns. as low as  $10^{-12}$  M causes primary cultures of osteoblasts to produce bone in vitro. This effect is not found with  $1,25(\text{OH})_2\text{D}_3$  even at  $10^{-8}$  M, suggesting that 2MD might be osteogenic in vivo. Indeed, 2MD (7 pmol/day) causes a substantial increase (9%) in total body bone mass in ovariectomized rats over a 23-wk period.  $1,25(\text{OH})_2\text{D}_3$  (500 pmol three times a week) only prevented the bone loss associated with ovariectomy and did not increase bone mass. These results indicate that 2MD is a potent bone-selective analog of  $1,25(\text{OH})_2\text{D}_3$  potentially effective in treating bone loss diseases.  
 IT 213250-70-5  
 RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (dihydroxyvitamin D3 analog effects on bone metabolism and induction of bone formation)  
 RN 213250-70-5 HCAPLUS  
 CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, ( $1\alpha,3\beta,7\text{E},20\text{S}$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



## RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Blunt, J	1968	61	1503	Proc Natl Acad Sci U	HCAPLUS

Carlsson, A	1952	26	212	Acta Physiol Scand	HCAPLUS
DeLuca, H	1981	75	333	Harvey Lect	HCAPLUS
Denhardt, D	1998	30-31	92	J Cell Biochem	
Kong, Y	1999	397	315	Nature	HCAPLUS
Lamm, M	1958	66	204	Arch Pathol	HCAPLUS
Li, Y	1998	139	4391	Endocrinology	HCAPLUS
Liu, Y	2000	14	1776	Mol Endocrinol	HCAPLUS
Morony, S	1999	14	1478	J Bone Miner Res	HCAPLUS
Orimo, H	1987	3	47	Bone Miner	MEDLINE
Paaren, H	1977		890	J Chem Soc Chem Comm	HCAPLUS
Perlman, K	1990	29	190	Biochemistry	HCAPLUS
Rodan, G	1996		289	Osteoporosis	
Shen, J	2002	277	20284	J Biol Chem	HCAPLUS
Shevde, N	2001	38	606	Cleft Palate Craniof	MEDLINE
Shevde, N	2000	97	7829	Proc Natl Acad Sci U	HCAPLUS
Shipley, P	1925	30	37	Am J Dis Child	
Sicinski, R	1998	41	4662	J Med Chem	HCAPLUS
Simonet, W	1997	89	309	Cell	HCAPLUS
Suda, T	1970	100	1049	J Nutr	HCAPLUS
Takahashi, N	1988	123	2600	Endocrinology	HCAPLUS
Tilyard, M	1992	326	357	N Engl J Med	MEDLINE
Underwood, J	1984	246	E493	Am J Physiol	HCAPLUS
Yang, W	1999	274	16838	J Biol Chem	HCAPLUS
Zierold, C	1994	91	900	Proc Natl Acad Sci U	HCAPLUS

L30 ANSWER 12 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:387626 HCAPLUS

DN 136:401925

TI Preparation of 26,27-homologated-20-epi-2-alkylidene-19-nor-vitamin D compounds as antiosteoporotics and antitumor agents

IN Deluca, Hector F.; Sicinski, Rafal R.

PA Wisconsin Alumni Research Foundation, USA

SO U.S., 22 pp., Cont.-in-part of U.S. Ser. No. 370,966, abandoned.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6392071	B1	20020521	US 2000-540686	20000331
	US 5843928	A	19981201	US 1997-819693	19970317
	US 5936133	A	19990810	US 1998-151113	19980910
	WO 2001074766	A1	20011011	WO 2001-US10317	20010329
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1268416	A1	20030102	EP 2001-920897	20010329
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2003529581	T2	20031007	JP 2001-572461	20010329
	US 2002087015	A1	20020704	US 2001-1711	20011031
	US 6537981	B2	20030325		
	US 2003181427	A1	20030925	US 2003-352745	20030128
	US 6696431	B2	20040224		
	US 2004167104	A1	20040826	US 2004-780103	20040217
PRAI	US 1997-819693	A3	19970317		
	US 1998-151113	A1	19980910		



US 1999-370966	B2	19990810
US 2000-540686	A	20000331
WO 2001-US10317	W	20010329
US 2001-1711	A3	20011031
US 2003-352745	A3	20030128

OS MARPAT 136:401925  
GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Novel vitamin D related compds., namely, 2-alkylidene-19-nor-vitamin D derivs. of formula I [Y1, Y2 = H, protecting group; R6, R8 = alkyl, hydroxyalkyl, fluoroalkyl, etc., or when taken together represent the group -(CH2)x- where x is an integer from 2 to 5; R = any of the typical side chains known for vitamin D type compds.] are prepared. These 2-substituted compds. are characterized by low intestinal calcium transport activity and high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. Thus, 20(S)-1 $\alpha$ ,25-dihydroxy-2-methylene-26,27-dihomo-19-nor-vitamin D3 (II) was prepared via a multistep synthetic sequence starting from 20(S)-25-hydroxy Grundmann's ketone analog III and phosphine oxide IV. The intestinal calcium transport and serum calcium (bone calcium mobilization) activities in vitamin D-deficient rats on a low calcium diet responding to chronic doses of II at 15 pmol/day/7 days were 4.0  $\pm$  0.4 S/M and 5.3  $\pm$  0.1 S/M resp. These compds. also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

IT 213250-70-5P 213319-29-0P

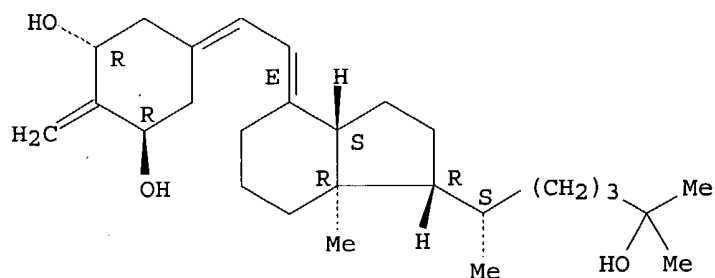
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 26,27-homologated-20-epi-2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

RN 213250-70-5 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 $\alpha$ ,3 $\beta$ ,7E,20S)- (9CI) (CA INDEX NAME)

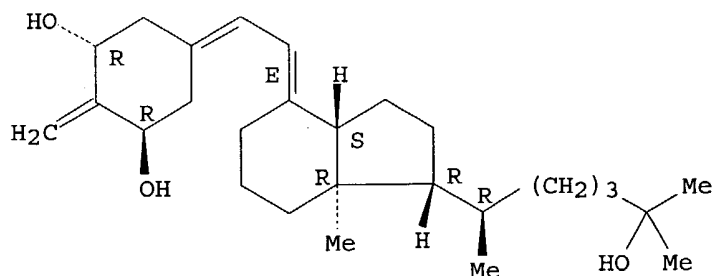
Absolute stereochemistry.  
Double bond geometry as shown.



RN 213319-29-0 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 $\alpha$ ,3 $\beta$ ,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



## RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Anon	1998			WO 9841501	HCAPLUS
Deluca	1989			US 4800198 A	HCAPLUS
Deluca	1989			US 4851401 A	HCAPLUS
Deluca	1992			US 5089641 A	HCAPLUS
Deluca	1996			US 5587497 A	HCAPLUS
Deluca	1999			US 5945410 A	HCAPLUS
Deluca	1999			US 5981780 A	HCAPLUS
Paaren	1999			US 5936105 A	HCAPLUS
Sicinski	1998		4662	J Med Chem	HCAPLUS
Yang	1999		16838	Journal of Biologica	HCAPLUS

L30 ANSWER 13 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:332679 HCAPLUS

DN 136:335278

TI 1 $\alpha$ -Hydroxy-2-methylene-19-nor-homopregnacalciferol and its  
therapeutic usesIN DeLuca, Hector F.; Sicinski, Rafal R.; Gowlugari, Sumithra;  
Plum, Lori A.; Claggett-Dame, Margaret

PA USA

SO U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of U. S. Ser. No. 657,828.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002052350	A1	20020502	US 2001-878438	20010611
	US 6440953	B2	20020827		
	US 2002183289	A1	20021205	US 2002-165123	20020607
	US 6579861	B2	20030617		
PRAI	US 2000-657828	A2	20000908		
	US 2001-878438	A3	20010611		

AB The invention discloses 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and its pharmaceutical uses. This compound exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. This compound also has little, if any, calcemic activity and therefore may be used to treat immune disorders in humans as well as renal osteodystrophy.

IT 213250-70-5

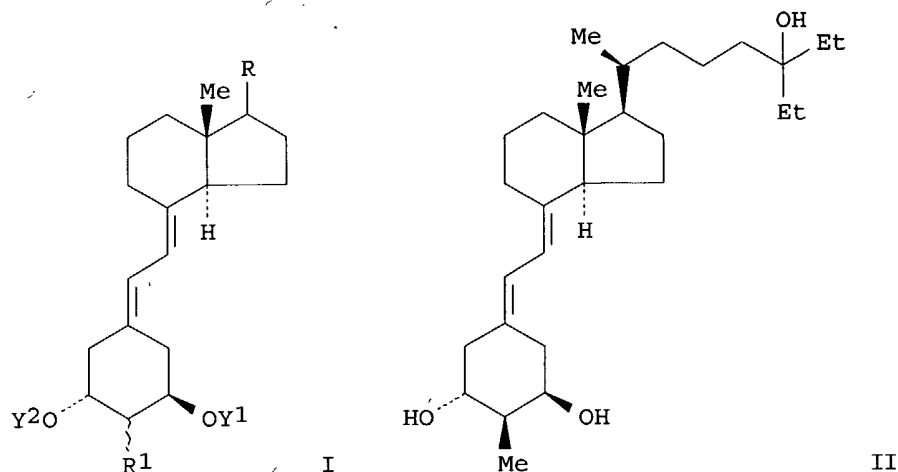
RL: PAC (Pharmacological activity); BIOL (Biological study)  
(hydroxymethylenenorhomopregnacalciferol and therapeutic use)

RN 213250-70-5 HCAPLUS

CN 19-Nor-9,10-secholesta-5,7-diene-1,3,25-triol, 2-methylene-,



OS MARPAT 135:358086  
GI



AB 2-Alkyl-19-nor-vitamin D derivs. of formula I [Y1, Y2 = H, protecting group; R = typical side chains known for vitamin D type compds.; R1 = alkyl, hydroxyalkyl, fluoroalkyl] are prepared. These 2-substituted compds., especially the 2 $\alpha$ -Me and the 2 $\alpha$ -methyl-20S derivs., are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compds. also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anticancer agents and for the treatment of diseases such as psoriasis. Thus, II was prepared and showed preferential activity on bone in biol. activity tests.

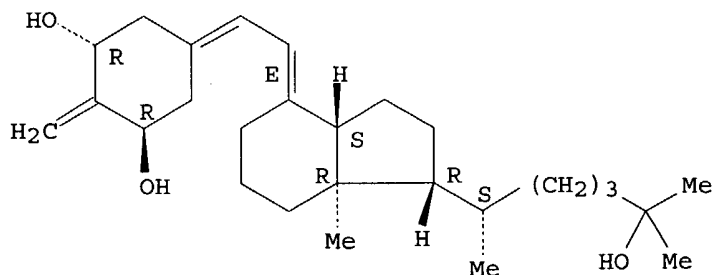
IT 213250-70-5P 213319-29-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of 26,27-homologated-20-epi-2-alkyl-19-norvitamin D compds. with high intestinal calcium transport activity)

RN 213250-70-5 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E,20S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



RN 213319-29-0 HCAPLUS

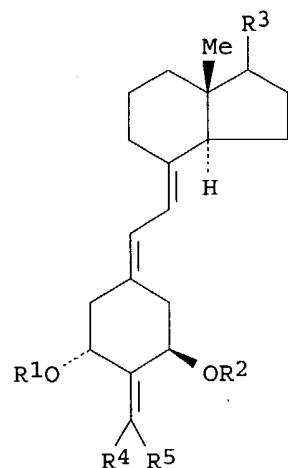
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,



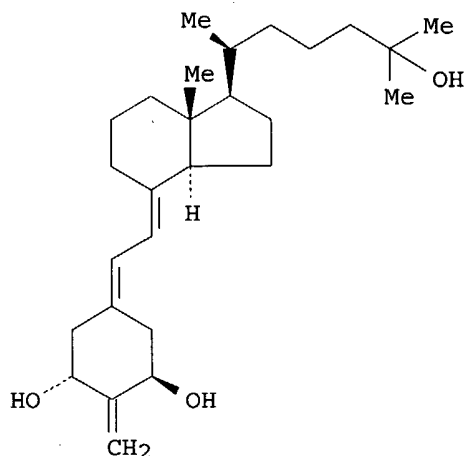
LA English

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001074766	A1	20011011	WO 2001-US10317	20010329
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	US 6392071	B1	20020521	US 2000-540686	20000331
	EP 1268416	A1	20030102	EP 2001-920897	20010329
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2003529581	T2	20031007	JP 2001-572461	20010329
PRAI	US 2000-540686	A	20000331		
	US 1997-819693	A3	19970317		
	US 1998-151113	A1	19980910		
	US 1999-370966	B2	19990810		
	WO 2001-US10317	W	20010329		
OS	MARPAT 135:288953				
GI					



I



II

AB Novel vitamin D related compds., namely, 2-alkylidene-19-nor-vitamin D derivs. of formula I [R<sub>1</sub>, R<sub>2</sub> = H, protecting group; R<sub>3</sub> = typical side chains known for vitamin D type compds.; R<sub>4</sub>, R<sub>5</sub> = H, alkyl, hydroxyalkyl, fluoroalkyl, etc.; R<sub>4</sub>R<sub>5</sub> = cycloalkylidene] are prepared. These 2-substituted compds. are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compds. also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anticancer agents and for the treatment of diseases such as psoriasis. Thus, II is prepared and is found to be extremely potent in inducing differentiation of HL-60 cells.

IT 213250-70-5P 213319-29-OP

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

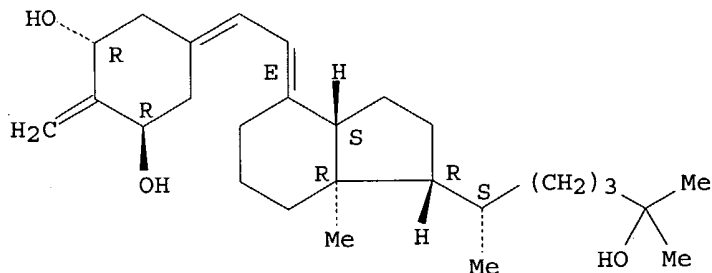
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);  
 BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of 2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics  
 and antitumor agents)

RN 213250-70-5 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
 (1 $\alpha$ ,3 $\beta$ ,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

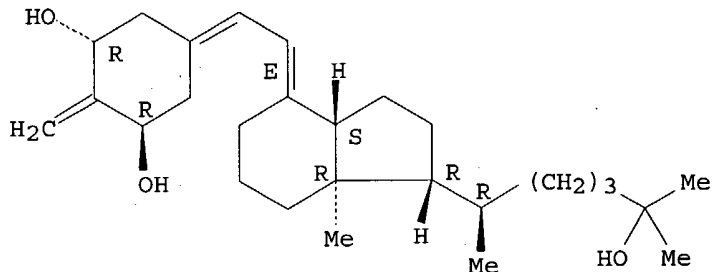


RN 213319-29-0 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
 (1 $\alpha$ ,3 $\beta$ ,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



#### RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Deluca, H	1989			US 4851401 A	HCAPLUS
Deluca, H	1999			US 5981780 A	HCAPLUS
Sicinski	1998	41	4662	JOURNAL OF MEDICINAL	HCAPLUS
Wisconsin Alumni Res Fo	1998			WO 9841501 A	HCAPLUS
Yang	1999	274	16838	J BIOL CHEM	HCAPLUS

L30 ANSWER 16 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:747742 HCAPLUS

DN 135:304063

TI Preparation of 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compounds

IN Deluca, Hector F.; Sicinski, Rafal R.

PA Wisconsin Alumni Research Foundation, USA

SO PCT Int. Appl., 74 pp.

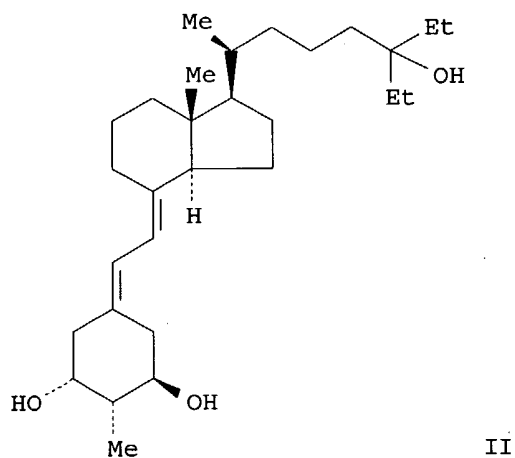
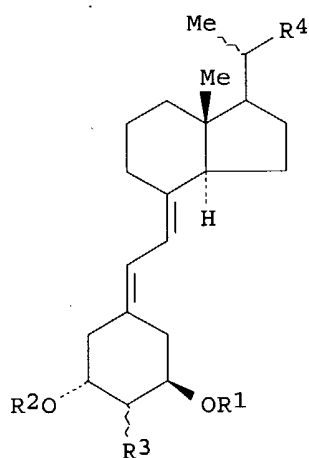
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001074765	A1	20011011	WO 2001-US10094	20010329
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6316642	B1	20011113	US 2000-541470	20000331
	EP 1268415	A1	20030102	EP 2001-920863	20010329
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004500414	T2	20040108	JP 2001-572460	20010329
	US 2004072804	A1	20040415	US 2003-673618	20030929
PRAI	US 2000-541470	A	20000331		
	US 1997-819694	A2	19970317		
	US 1998-135463	A3	19980817		
	US 1999-454013	A2	19991203		
	WO 2001-US10094	W	20010329		
	US 2001-45941	B3	20011019		
OS	MARPAT 135:304063				
GI					



AB 2-Alkyl-19-nor-vitamin D derivs. of formula I [R1, R2 = H, protecting group; R3 = alkyl, hydroxyalkyl, fluoroalkyl; R4 = H, Me, acyl, OH, any of the typical side chains known for vitamin D type compds., etc.] are prepared These compds. are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compds. also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis. Thus, II is prepared and had a VDR binding ratio of 5.5, and HL-60 differentiation ED50 of  $1.1 \times 10^{-10}$  M.

IT 213250-70-5P 213319-29-0P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compds. as



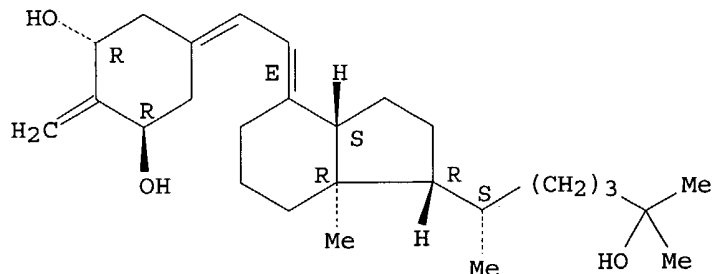
antiosteoporotics and antitumor agents)

RN 213250-70-5 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

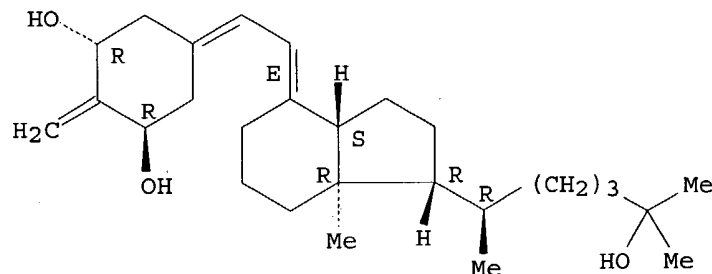


RN 213319-29-0 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



# RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Mikami, K	1999	12	1899	SYNLETT	
Sicinski, R	1998	41	4662	J MED CHEM	HCAPLUS
Wisconsin Alumni Resear	2000			WO 0010548 A	
Wisconsin Alumni Resear	1990			WO 9000541 A	HCAPLUS
Wisconsin Alumni Resear	1998			WO 9841500 A	HCAPLUS

L30 ANSWER 17 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2000:699222 HCAPLUS

DN 133:267021

TI preparation and therapeutic use of 2-alkyl-19-nor-vitamin D derivatives

IN Deluca, Hector F.; Sicinski, Rafal R.

PA Wisconsin Alumni Research Foundation, USA

SO U.S., 27 pp., Cont.-in-part of U.S. 5,945,410.

CODEN: USXXAM

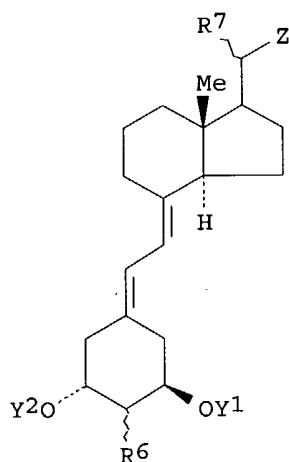
DT Patent

LA English

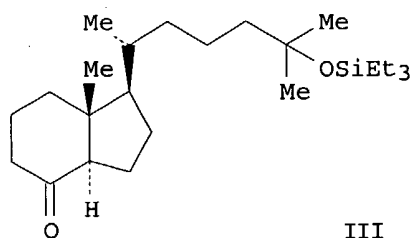
FAN.CNT 6

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6127559	A	20001003	US 1998-135463	19980817

US 5945410	A	19990831	US 1997-819694	19970317
PT 971888	T	20040331	PT 1998-905101	19980211
ES 2206893	T3	20040516	ES 1998-905101	19980211
US 6277837	B1	20010821	US 1999-454013	19991203
US 6316642	B1	20011113	US 2000-541470	20000331
US 6306844	B1	20011023	US 2000-616778	20000714
US 2002151528	A1	20021017	US 2001-45941	20011019
US 2002123638	A1	20020905	US 2001-999299	20011031
US 6544969	B2	20030408		
US 2003073857	A1	20030417	US 2002-246968	20020919
US 6667298	B2	20031223		
US 2004072804	A1	20040415	US 2003-673618	20030929
US 2004082802	A1	20040429	US 2003-683330	20031010
PRAI US 1997-819694	A2	19970317		
US 1998-135463	A3	19980817		
US 1999-454013	A2	19991203		
US 2000-541470	A3	20000331		
US 2000-616778	A3	20000714		
JP 2001-83085	A	20010322		
US 2001-45941	B3	20011019		
US 2001-999299	A3	20011031		
US 2002-246968	A3	20020919		
OS MARPAT 133:267021				
GI				



I



III

AB This invention discloses a novel class of vitamin D related compds., namely, the 2-alkyl-19-nor-vitamin D derivs. (I) (Y1,Y2 = H, hydroxy-protecting group; R6 = alkyl, hydroxyalkyl, fluoroalkyl; R7 =  $\alpha$  or  $\beta$ -Me; Z = Y, -OY, -CH2OY, -C.tplbond.CY, -CH=CHY (Y = H, Me, -(CH2)m-C(R1R2)-(CH2)n-C(R3R4R5); where m and n, independently integers from 0-5; R1 = H, OH, protected hydroxy, F, CF3, alkyl etc., R2, R3, R4 = D, deuterioalkyl, H, F, CF3, alkyl etc., R1+R2 = O, =C(R2R3) etc., R5 = H, OH, protected hydroxy, alkyl, and wherein any of the CH-groups at position 20,22, or 23 in the side chain may be replaced by a N atom or where any of the groups -CH(Me)-, -CH(R3)-, or -CH(R2)- at positions 20, 22, and 23, resp., may be replaced by an oxygen or sulfur atom)), were prepared Thus, I (Y1,Y2 = H; R6,R7 =  $\alpha$ -Me; Z = (CH2)3C(Me)2OH) (II) was prepared starting from Me quinicite and followed by Wittig-Horner coupling with Grundman's ketone (III). The 2-substituted compds., especially the 2 $\alpha$ -Me and the 2 $\alpha$ -methyl-20S derivs., are characterized by relatively low intestinal calcium transport activity and high bone calcium mobilization activity resulting in novel therapeutic agents for the

treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. I also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

## IT 213250-70-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

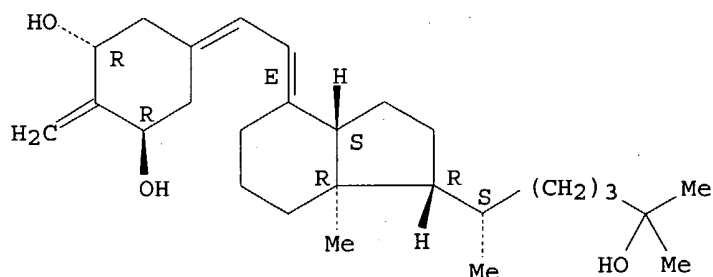
(preparation and therapeutic use of 2-alkyl-19-nor-vitamin D analog)

RN 213250-70-5 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E,20S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



## IT 213319-29-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

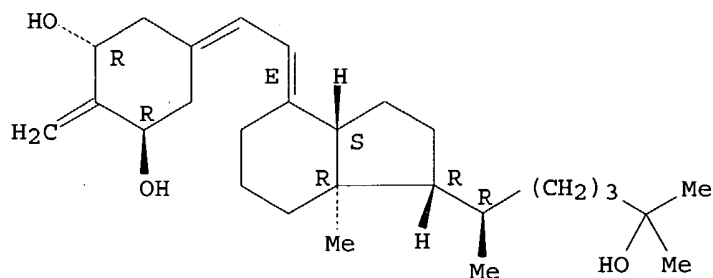
(preparation and therapeutic use of 2-alkyl-19-nor-vitamin D analog)

RN 213319-29-0 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



## RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
=====	=====	=====	=====	=====	=====
Anon	1985			EP 0184206	HCAPLUS
Anon	1990			EP 0387077	HCAPLUS
Anon	1992			EP 0516410	HCAPLUS
Deluca	1992			US 5086191	HCAPLUS
Miyamoto	1987			US 4666634	HCAPLUS
Posner	1991	56	4339	J Org Chem	HCAPLUS

L30 ANSWER 18 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1999:505692 HCAPLUS  
 DN 131:144749  
 TI Preparation of 14-epi-19-nor-vitamin D compounds with cell differentiation activity  
 IN Paaren, Herbert E.  
 PA Tetrionics, Inc., USA  
 SO U.S., 14 pp.  
 CODEN: USXXAM  
 DT Patent  
 LA English  
 FAN.CNT 1

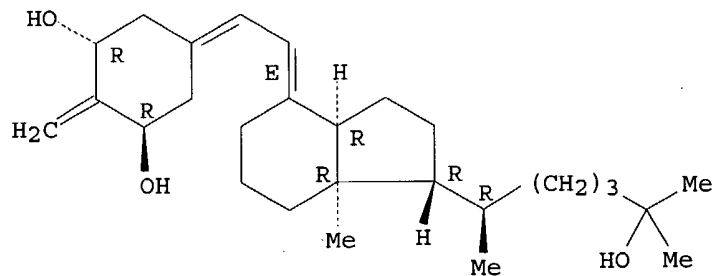
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5936105	A	19990810	US 1998-96330	19980611
PRAI	US 1997-53088P	P	19970613		

AB 14-Epi-19-nor-vitamin D analog compds. are prepared with high cell differentiation and antiproliferative activity and low calcemic activity. More particularly, examples of such compds. include 14-epi-19-nor-1 $\alpha$ ,25-dihydroxyvitamin D3, 14-epi-20-epi-19-nor-1 $\alpha$ ,25-dihydroxyvitamin D3 (I), 14-epi-20-epi-19-nor-1 $\alpha$ -hydroxyvitamin D3, 14-epi-19-nor-1 $\alpha$ ,25-dihydroxyvitamin D2, 14-epi-19-nor-24-homo-1 $\alpha$ ,25-dihydroxyvitamin D3, 14-epi-19-nor-20(S)-hydroxymethyl-1 $\alpha$ -hydroxypregnacalciferol, and 14-epi-19-nor-20(R)-hydroxymethyl-1 $\alpha$ -hydroxypregnacalciferol. Thus, I was prepared and showed an EC50 of 0.66 nM to inhibit proliferation of HL-60 cells.

IT 235108-14-2P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of 14-epi-19-nor-vitamin D compds. with cell differentiation activity)

RN 235108-14-2 HCAPLUS  
 CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 $\alpha$ ,3 $\beta$ ,7E,14 $\beta$ ) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



RETABLE						
Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File	
DeLuca	1995			US 5391755	HCAPLUS	
DeLuca	1998			US 5843928	HCAPLUS	

L30 ANSWER 19 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1998:672847 HCAPLUS  
 DN 130:52625  
 TI New 1 $\alpha$ ,25-Dihydroxy-19-norvitamin D3 Compounds of High Biological

Activity: Synthesis and Biological Evaluation of 2-Hydroxymethyl, 2-Methyl, and 2-Methylene Analogs

AU Sicinski, Rafal R.; Prahl, Jean M.; Smith, Connie M.; DeLuca, Hector F.

CS Department of Biochemistry College of Agricultural and Life Sciences, University of Wisconsin-Madison, Madison, WI, 53706, USA

SO Journal of Medicinal Chemistry (1998), 41(23), 4662-4674  
CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

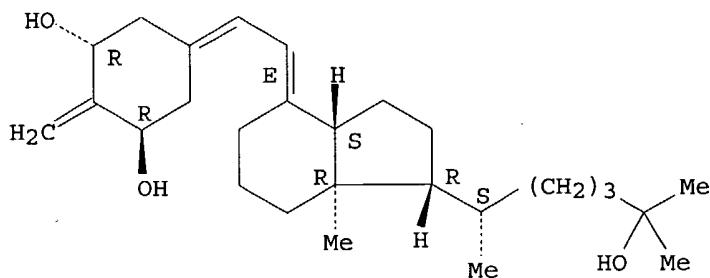
AB New highly active isomers of the natural hormone  $1\alpha,25$ -dihydroxyvitamin D<sub>3</sub> possessing an exomethylene group at the 2-position were prepared in a convergent manner, starting with (-)-quinic acid and the corresponding (20R)- and (20S)-25-hydroxy Grundmann ketones. These 2-methylene-19-norvitamins were efficiently converted to the 2-Me and 2-hydroxymethyl derivs., some of which exhibited pronounced in vivo biol. activity. Configurations of the A-ring substituents were determined by <sup>1</sup>H NOE difference spectroscopy as well as by spin decoupling expts. It was established that the bulky Me and hydroxymethyl substituents at C-2, due to their large conformational free energies, occupy mainly equatorial positions. Addnl., hydroxylation of the C(10)-C(19) double bond in  $1\alpha,25$ -(OH)<sub>2</sub>D<sub>3</sub> was performed, resulting in  $1\alpha,19,25$ -trihydroxy-10,19-dihydrovitamin D<sub>3</sub> derivs. in which the hydroxymethyl substituent at C-10, for steric reasons, is forced to occupy an axial position. In consequence, the vitamin D<sub>3</sub> analogs were synthesized in which the  $1\alpha$ -hydroxy group, required for biol. activity, is almost exclusively axially or equatorially oriented because of stabilization of the single A-ring chair conformations. The relative ability of the synthesized analogs to bind the porcine intestinal vitamin D receptor was assessed and compared with that of the natural hormone. It was established that vitamins possessing the axial orientation of the  $1\alpha$ -hydroxy substituent exhibit a significantly increased receptor binding affinity. Compds. with a 2-methylene substituent showed selective calcemic activity profiles, being extremely effective on bone calcium mobilization.  $2\alpha$ -Methyl-substituted vitamins proved to be much more active in vivo than the corresponding epimers with  $2\beta$ -configuration. All of the 2-substituted vitamins exhibited pronounced HL-60 differentiating activity, those  $2\alpha$ -substituted in the 20S-series being especially potent. The present studies imply that the axial orientation of the  $1\alpha$ -hydroxy group is necessary for biol. activity of vitamin D compds.

IT 213250-70-5P 213319-29-0P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)  
(synthesis and biol. evaluation of 2-hydroxymethyl, 2-Me, and 2-methylene  $1\alpha,25$ -dihydroxy-19-norvitamin D<sub>3</sub> analogs)

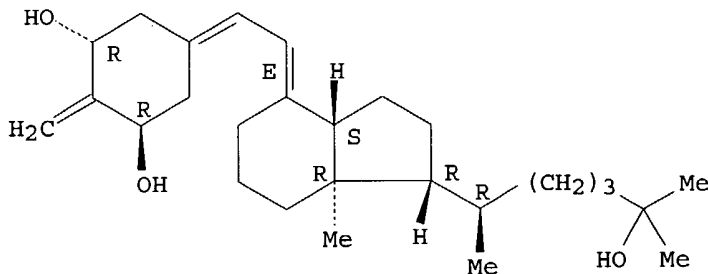
RN 213250-70-5 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, ( $1\alpha,3\beta,7E,20S$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



RN 213319-29-0 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E)- (9CI) (CA INDEX NAME)Absolute stereochemistry.  
Double bond geometry as shown.

## RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Anet, F	1962	84	1053	J Am Chem Soc	HCAPLUS
Berman, E	1978	100	5626	J Am Chem Soc	HCAPLUS
Berman, E	1977	42	3325	J Org Chem	MEDLINE
Binderup, L	1991	42	1569	Biochem Pharmacol	HCAPLUS
Bouillon, R	1995	16	200	Endocr Rev	HCAPLUS
Dame, M	1986	25	4523	Biochemistry	HCAPLUS
Deluca, H				EP 387077	HCAPLUS
Deluca, H	1984	19	179	Annu Rep Med Chem	HCAPLUS
Deluca, H	1991	3	1129	Comprehensive Medici	
Deluca, H	1988	2	224	FASEB J	HCAPLUS
Deluca, H	1974	33	2211	Fed Proc	HCAPLUS
Deluca, H	1979	83	1	Top Curr Chem	HCAPLUS
Eguchi, T	1990	18	19	Bioorg Chem	HCAPLUS
Eguchi, T	1991	19	327	Bioorg Chem	HCAPLUS
Eliel, E	1965		355	Conformational Analy	
Havinga, E	1973	29	1181	Experientia	HCAPLUS
Helmer, B	1985	241	608	Arch Biochem Biophys	HCAPLUS
Hirsch, J	1967	1	199	Top Stereochem	HCAPLUS
Ikekawa, N	1987	7	333	Med Res Rev	HCAPLUS
Ikekawa, N	1987	7	333	Med Res Rev	HCAPLUS
Ishida, H	1995	60	1828	J Org Chem	HCAPLUS
Johnson, F	1968	68	375	Chem Rev	HCAPLUS
Johnson, F	1965	87	5492	J Am Chem Soc	HCAPLUS
Jones, G	1987	49	29	Steroids	HCAPLUS
Konno, K	1998	8	151	Bioorg Med Chem Lett	HCAPLUS
Kragballe, K	1992	49	46	J Cell Biochem	HCAPLUS
Lythgoe, B	1981		449	Chem Soc Rev	

Lythgoe, B	1976		2386	J Chem Soc Perkin Tr	HCAPLUS
Lythgoe, B	1978		590	J Chem Soc Perkin Tr	HCAPLUS
MacLaughlin, J	1985	82	5409	Proc Natl Acad Sci U	HCAPLUS
Miyamoto, K				EP 184206	HCAPLUS
Miyamoto, K	1993	41	1111	Chem Pharm Bull	HCAPLUS
Miyaura, C	1981	102	937	Biochem Biophys Res	HCAPLUS
Morimoto, S	1986	38	119	Calcif Tissue Int	MEDLINE
Mourino, A	1978	43	1653	J Org Chem	HCAPLUS
Narwid, T	1974	57	771	Helv Chim Acta	HCAPLUS
Nasipuri, D	1991		270	Stereochemistry of o	
Nordin, B	1992	49	19	J Cell Biochem	HCAPLUS
Norman, A	1994			Vitamin D, a pluripo	
Norman, A	1979			Vitamin D the calciu	
Okamura, W	1977	42	2284	J Org Chem	HCAPLUS
Okamura, W	1978	43	574	J Org Chem	HCAPLUS
Okamura, W	1995	53	603	J Steroid Biochem Mo	HCAPLUS
Okamura, W	1974	71	4194	Proc Natl Acad Sci U	HCAPLUS
Okamura, W	1975		4317	Tetrahedron Lett	HCAPLUS
Okano, T	1989	163	1444	Biochem Biophys Res	HCAPLUS
Ostrem, V	1987	262	14164	J Biol Chem	HCAPLUS
Ostrem, V	1987	49	73	Steroids	HCAPLUS
Paaren, H	1985	13	62	Bioorg Chem	HCAPLUS
Perlman, K	1990	31	1823	Tetrahedron Lett	HCAPLUS
Perlman, K	1991	32	7663	Tetrahedron Lett	HCAPLUS
Posner, G	1994	59	7855	J Org Chem	HCAPLUS
Posner, G	1995	60	4617	J Org Chem	HCAPLUS
Reichel, H	1989	320	980	N Engl J Med	HCAPLUS
Schlosser, M	1976	30	197	Chimia	HCAPLUS
Sheves, M	1975		643	J Chem Soc Chem Comm	HCAPLUS
Sheves, M	1977	42	3597	J Org Chem	HCAPLUS
Sicinski, R	1994	22	150	Bioorg Chem	HCAPLUS
Sicinski, R	1994	37	3730	J Med Chem	HCAPLUS
Snedecor, G	1967			Statistical Methods	
Stoddart, J	1971		64	Stereochemistry of c	
Suda, T	1990	10	195	Annu Rev Nutr	HCAPLUS
Suda, T	1970	100	1049	J Nutr	HCAPLUS
Suda, T	1989	191	214	Proc Soc Exp Biol Me	HCAPLUS
Tsoukas, C	1984	224	1438	Science (Washington,	HCAPLUS
Uhland-Smith, A	1993	123	1777	J Nutr	HCAPLUS
van der Kerkhof, P	1995	132	675	Br J Dermatol	
Wecksler, W	1980	35	419	Steroids	HCAPLUS
Wing, R	1975	97	4980	J Am Chem Soc	HCAPLUS
Winstein, S	1955	77	5562	J Am Chem Soc	HCAPLUS

L30 ANSWER 20 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1998:635741 HCAPLUS

DN 129:245333

TI Preparation of 2-alkylidene-19-nor-vitamin D compounds

IN Deluca, Hector F.; Sicinski, Rafal R.

PA Wisconsin Alumni Research Foundation, USA

SO PCT Int. Appl., 61 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO 9841501	A1	19980924	WO 1998-US2976	19980211
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,				
	DK, EE, ES, FI, GB, GE, GH, GW, HU, IL, IS, JP, KE, KG, KP, KR,				
	KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ,				
	PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG,				
	UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,  
 FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,  
 GA, GN, ML, MR, NE, SN, TD, TG

US 5843928	A	19981201	US 1997-819693	19970317
AU 9862801	A1	19981012	AU 1998-62801	19980211
AU 714253	B2	19991223		
EP 970047	A1	20000112	EP 1998-905102	19980211
EP 970047	B1	20020911		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NZ 337503	A	20000929	NZ 1998-337503	19980211
JP 2001504135	T2	20010327	JP 1998-540501	19980211
AT 223890	E	20020915	AT 1998-905102	19980211
ES 2179451	T3	20030116	ES 1998-905102	19980211
PT 970047	T	20030131	PT 1998-905102	19980211
NO 9904398	A	19990910	NO 1999-4398	19990910
PRAI US 1997-819693	A	19970317		
WO 1998-US2976	W	19980211		
OS MARPAT 129:245333				
GI				

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The title compds. [I; Y1, Y2 = H, protecting group; R6, R8 = H, alkyl, hydroxyalkyl, fluoroalkyl, or R6R8 = (CH2)x; x = 2-5 integer; R = any of the typical side chains known for vitamin D type compds., e.g. Q] are prepared Thus, 1 $\alpha$ ,25-dihydroxy-2-methylene-19-norvitamin D3 (II) was prepared in 11 steps from (-)-quinic acid via tert-butyldimethylsilyl protection of the OH groups at the 3 and 5 positions, converting to protected quinic acid Me ester, oxidation of the 4-OH, methylenation using methyltriphenylphosphonium bromide, hydride reduction, NaIO4 oxidation, condensation of 3,5-bis(tert-butyldimethylsilyloxy)-4-methylenecyclohexanone with Me3SiCH2-COOMe, DIBAL reduction, reaction with Ph2PH, H2O2 oxidation, condensation with perhydroindanone III in the presence of BuLi, and deprotection. These 2-substituted compds. are characterized by low intestinal calcium transport activity and high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. The intestinal calcium transport and serum calcium (bone calcium mobilization) activities in rats responding to chronic doses of II at 130 pmol/day/7 days were 5.3 $\pm$ 0.4 S/M and 9.9 $\pm$ 0.2 mg/100 mL, resp., vs. 6.2 $\pm$ 0.4 S/M and 7.2 $\pm$ 0.5 mg/100 mL, resp., for 1,25-(OH)2D3. These compds. also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

IT 213250-70-5P

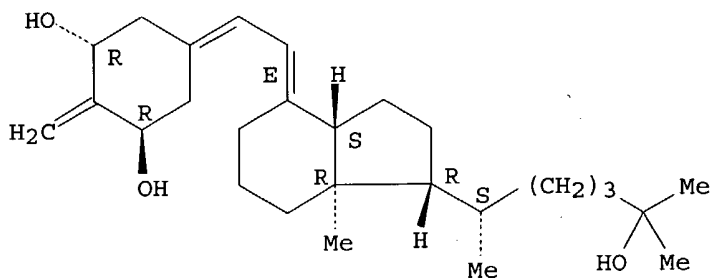
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of 2-alkylidenenor-vitamin D compds.)

RN 213250-70-5 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
 (1 $\alpha$ ,3 $\beta$ ,7E,20S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.





## RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Chugai Pharmaceutical C	1994			JP 06041059 A	HCAPLUS
Deluca, H	1996			US 5536713 A	HCAPLUS
Miyamoto, K	1987			US 4666634 A	HCAPLUS
The John-Hopkins Univer	1996			WO 9601811 A	HCAPLUS

L30 ANSWER 21 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1998:635740 HCAPLUS

DN 129:245332

TI Preparation of 2-alkyl-19-nor-vitamin D compounds and their biological activities

IN Deluca, Hector F.; Sicinski, Rafal R.

PA Wisconsin Alumni Research Foundation, USA

SO PCT Int. Appl., 55 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 6

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9841500	A1	19980924	WO 1998-US2975	19980211
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GW, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5945410	A	19990831	US 1997-819694	19970317
AU 9862800	A1	19981012	AU 1998-62800	19980211
AU 714390	B2	19991223		
EP 971888	A1	20000119	EP 1998-905101	19980211
EP 971888	B1	20031029		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9808010	A	20000308	BR 1998-8010	19980211
NZ 337262	A	20000929	NZ 1998-337262	19980211
JP 2000513010	T2	20001003	JP 1998-540500	19980211
AT 253046	E	20031115	AT 1998-905101	19980211
PT 971888	T	20040331	PT 1998-905101	19980211
ES 2206893	T3	20040516	ES 1998-905101	19980211
NO 9904489	A	19990916	NO 1999-4489	19990916
US 2004072804	A1	20040415	US 2003-673618	20030929
PRAI US 1997-819694	A	19970317		
WO 1998-US2975	W	19980211		
US 2001-45941	B3	20011019		

OS MARPAT 129:245332  
GI

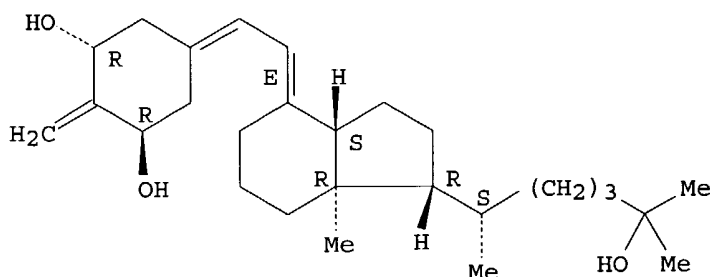
\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The title compds. [I; Y1, Y2 = H, protecting group; R6 = alkyl, hydroxyalkyl, fluoroalkyl, etc.; R = any of the typical side chains known for vitamin D type compds., e.g. Q] are prepared Thus, 1 $\alpha$ ,25-dihydroxy-2 $\alpha$ - and 1 $\alpha$ ,25-dihydroxy-2 $\beta$ -methyl-19-norvitamin D3 (II) were prepared in 11 steps from (-)-quinic acid via tert-butyldimethylsilyl protection of the OH groups at positions 3 and 5, converting to protected quinic acid Me ester, oxidation of the 4-OH, methylenation using methyltriphenylphosphonium bromide, hydride reduction, NaIO4 oxidation, condensation of the resulting 3,5-bis(tert-butyldimethylsilyloxy)-4-methylcyclohexanone with Me3SiCH2COOMe, DIBAL reduction, reaction with Ph2PH, oxidation, condensation with perhydroindanone

III in the presence of BuLi, and deprotection. These 2-substituted compds. are characterized by low intestinal calcium transport activity and high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. The intestinal calcium transport and serum calcium (bone calcium mobilization) activities in rats responding to chronic doses of II (both epimers) at 130 pmol/day/7 days were 5.0 $\pm$ 0.3 S/M and 6.1 $\pm$ 0.1 mg/100 mL, resp., vs. 6.2 $\pm$ 0.4 S/M and 7.2 $\pm$ 0.5 mg/100 mL, resp., for 1,25-(OH)2D3. These compds. also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

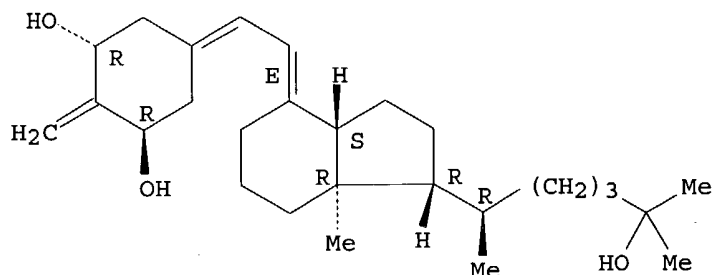
IT 213250-70-5P 213319-29-0P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of 2-alkylnor-vitamin D compds. and their biol. activities)  
RN 213250-70-5 HCAPLUS  
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 $\alpha$ ,3 $\beta$ ,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



RN 213319-29-0 HCAPLUS  
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 $\alpha$ ,3 $\beta$ ,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



## RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Chugai Pharmaceutical C	1994			JP 06041059 A	HCAPLUS
Deluca, H	1996			US 5536713 A	HCAPLUS
Miyamoto, K	1987			US 4666634 A	HCAPLUS
The John-Hopkins Univer	1996			WO 9601811 A	HCAPLUS

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FILE 'USPATFULL' ENTERED AT 13:51:17 ON 05 SEP 2004

CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 13:51:17 ON 05 SEP 2004

CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

=&gt; =&gt; d his l31-

(FILE 'USPATFULL, USPAT2' ENTERED AT 13:51:17 ON 05 SEP 2004)

L31 0 S L29 AND LIFE(L) EXPECT?  
 L32 2 S L29 AND (AGING? OR AGEING? OR LONGEV?)/CT,BI  
 L33 22 S L29 NOT L32

=&gt; d l32 bib abs kwic hitstr tot

L32 ANSWER 1 OF 2 USPATFULL on STN

AN 2004:89152 USPATFULL

TI Use of 2-methylene-19-nor-20(S)-1alpha,25-dihydroxyvitamin D3 to increase bone strength

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Smith, Connie M., Blue Mounds, WI, UNITED STATES

PI US 2004068129 A1 20040408

AI US 2003-673629 A1 20030929 (10)

RLI Division of Ser. No. US 2000-616164, filed on 14 Jul 2000, PENDING

DT Utility

FS APPLICATION

LREP ANDRUS, SCEALES, STARKE &amp; SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE 1100, MILWAUKEE, WI, 53202

CLMN Number of Claims: 29

ECL Exemplary Claim: 1

DRWN 7 Drawing Page(s)

LN.CNT 529

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides pharmaceutical uses for 2-methylene-19-nor-20(S)-1α,25-dihydroxyvitamin D.sub.3. This compound is characterized by high bone calcium mobilization activity demonstrating preferential activity on bone. This results in a novel therapeutic agent for the treatment of diseases where bone formation is desired, particularly osteoporosis. This compound also exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their

differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis. This compound also increases both breaking strength and crushing strength of bones evidencing use in conjunction with bone replacement surgery such as hip and knee replacements.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT **Aging, animal**

(senile osteoporosis; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)

IT 32222-06-3, 1 $\alpha$ ,25-Dihydroxyvitamin D3 **213319-29-0**

(methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)

IT **213250-70-5**

(methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)

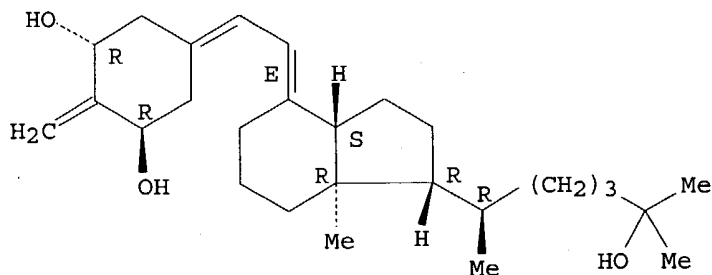
IT **213319-29-0**

(methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)

RN 213319-29-0 USPATFULL

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 $\alpha$ ,3 $\beta$ ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



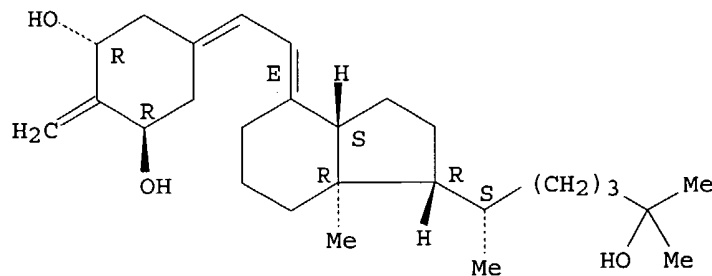
IT **213250-70-5**

(methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)

RN 213250-70-5 USPATFULL

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 $\alpha$ ,3 $\beta$ ,7E,20S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



L32 ANSWER 2 OF 2 USPATFULL on STN

AN 2003:277148 USPATFULL

TI Use of carbon-2-modified-vitamin D analogs to induce the formation of new bone  
 IN DeLuca, Hector F., Deerfield, WI, UNITED STATES  
 Pike, J. Wesley, Madison, WI, UNITED STATES  
 Shevde, Nirupama K., Madison, WI, UNITED STATES  
 PI US 2003195175 A1 20031016  
 AI US 2002-105826 A1 20020325 (10)  
 DT Utility  
 FS APPLICATION  
 LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE 1100, MILWAUKEE, WI, 53202  
 CLMN Number of Claims: 28  
 ECL Exemplary Claim: 1  
 DRWN 2 Drawing Page(s)  
 LN.CNT 1018

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB It has been discovered that the 2-carbon-modified derivatives of  $1\alpha,25$ -dihydroxyvitamin D<sub>3</sub> specifically stimulate osteoblasts to form new bone. The ability of the 2-carbon-modified vitamin D analogs to stimulate new bone formation suggest that these compounds can be used where synthesis of new bone is required. Thus, these compounds can be used either systemically or locally to stimulate the growth of bone transplants, to increase the rate of fracture healing and thereby reduce the time required for the healing of fractures, the stimulation of bone growth when required for replacement surgery, and also for the growth of bone to implants or other devices required to maintain the skeleton or teeth in the proper positions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . process that is homeostatic in nature and necessary for renewal of defective bone that occurs as a result of normal **aging** or trauma. This process is essential to the maintenance of adult skeletal integrity and is carried out through the activity. . .

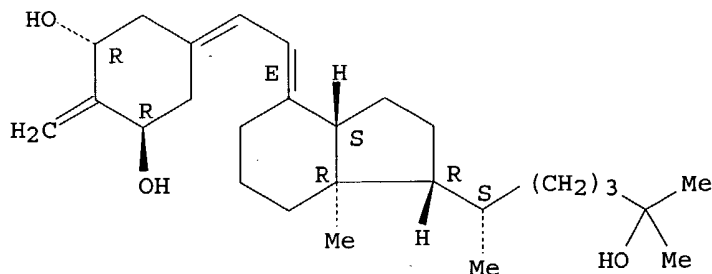
IT 32222-06-3,  $1\alpha,25$ -Dihydroxyvitamin D<sub>3</sub> 213250-70-5  
 606973-78-8 606973-79-9 606973-80-2 606973-81-3  
 (use of carbon-2-modified-vitamin D analogs to induce the formation of new bone)

IT 213250-70-5  
 (use of carbon-2-modified-vitamin D analogs to induce the formation of new bone)

RN 213250-70-5 USPATFULL

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
 ( $1\alpha,3\beta,7E,20S$ ) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



=> d 133 bib abs hitstr tot

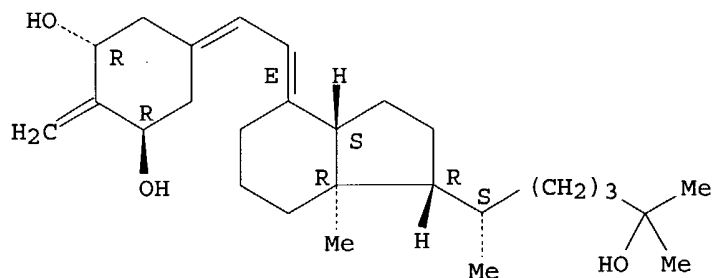
L33 ANSWER 1 OF 22 USPATFULL on STN  
AN 2004:108400 USPATFULL  
TI 26,27-Homologated-20-EPI-2-alkyl-19-nor-vitamin D compounds  
IN DeLuca, Hector F., Deerfield, WI, UNITED STATES  
Sicinski, Rafal R., Warsaw, POLAND  
PA Wisconsin Alumni Research Foundation, Madison, WI (U.S. corporation)  
PI US 2004082802 A1 20040429  
AI US 2003-683330 A1 20031010 (10)  
RLI Division of Ser. No. US 2002-246968, filed on 19 Sep 2002, GRANTED, Pat.  
No. US 6667298 Division of Ser. No. US 2001-999299, filed on 31 Oct  
2001, GRANTED, Pat. No. US 6544969 Division of Ser. No. US 2000-541470,  
filed on 31 Mar 2000, GRANTED, Pat. No. US 6316642 Continuation-in-part  
of Ser. No. US 1999-454013, filed on 3 Dec 1999, GRANTED, Pat. No. US  
6277837 Division of Ser. No. US 1998-135463, filed on 17 Aug 1998,  
GRANTED, Pat. No. US 6127559 Continuation-in-part of Ser. No. US  
1997-819694, filed on 17 Mar 1997, GRANTED, Pat. No. US 5945410  
DT Utility  
FS APPLICATION  
LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE  
1100, MILWAUKEE, WI, 53202  
CLMN Number of Claims: 46  
ECL Exemplary Claim: 1  
DRWN 6 Drawing Page(s)  
LN.CNT 2099  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AB This invention provides a novel class of vitamin D related compounds,  
namely, the 2-alkyl-19-nor-vitamin D derivatives, as well as a general  
method for their chemical synthesis. The compounds have the formula:  
##STR1##

where Y.sub.1 and Y.sub.2, which may be the same or different, are each  
selected from the group consisting of hydrogen and a hydroxy-protecting  
group, R.sub.6 is selected from the group consisting of alkyl,  
hydroxyalkyl and fluoroalkyl, and where the group R represents any of  
the typical side chains known for vitamin D type compounds. These  
2-substituted compounds, especially the 2 $\alpha$ -methyl and the  
2 $\alpha$ -methyl-20S derivatives, are characterized by relatively high  
intestinal calcium transport activity and relatively high bone calcium  
mobilization activity resulting in novel therapeutic agents for the  
treatment of diseases where bone formation is desired, particularly low  
bone turnover osteoporosis. These compounds also exhibit pronounced  
activity in arresting the proliferation of undifferentiated cells and  
inducing their differentiation to the monocyte thus evidencing use as  
anti-cancer agents and for the treatment of diseases such as psoriasis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

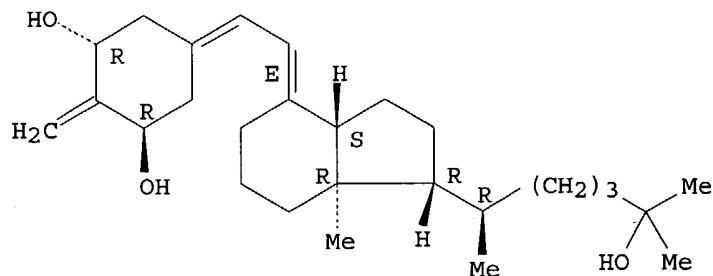
IT 213250-70-5P 213319-29-0P  
(preparation of 2-alkylnor-vitamin D compds. and their biol. activities)  
RN 213250-70-5 USPATFULL  
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E,20S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



RN 213319-29-0 USPATFULL  
 CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
 (1 $\alpha$ ,3 $\beta$ ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



L33 ANSWER 2 OF 22 USPATFULL on STN  
 AN 2004:95349 USPATFULL  
 TI Use of 2 $\alpha$ -methyl-19-nor-20(S)-1 $\alpha$ ,25-dihydroxyvitamin D3 to  
 increase bone strength  
 IN DeLuca, Hector F., Deerfield, WI, UNITED STATES  
 Smith, Connie M., Blue Mounds, WI, UNITED STATES  
 PA Wisconsin Alumni Research Foundation (U.S. corporation)  
 PI US 2004072804 A1 20040415  
 AI US 2003-673618 A1 20030929 (10)  
 RLI Division of Ser. No. US 2001-45941, filed on 19 Oct 2001, ABANDONED  
 DT Utility  
 FS APPLICATION  
 LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE  
 1100, MILWAUKEE, WI, 53202  
 CLMN Number of Claims: 29  
 ECL Exemplary Claim: 1  
 DRWN 3 Drawing Page(s)  
 LN.CNT 534  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 AB This invention provides pharmaceutical uses for 2 $\alpha$ -methyl-19-nor-  
 20(S)-1 $\alpha$ ,25-dihydroxyvitamin D.sub.3. This compound is  
 characterized by high bone calcium mobilization activity demonstrating  
 preferential activity on bone. This results in a novel therapeutic agent  
 for the treatment of diseases where bone formation is desired,  
 particularly osteoporosis. This compound also exhibits pronounced  
 activity in arresting the proliferation of undifferentiated cells and  
 inducing their differentiation to the monocyte thus evidencing use as an  
 anti-cancer agent and for the treatment of skin diseases such as  
 psoriasis. This compound also increases both breaking strength and  
 crushing strength of bones evidencing use in conjunction with bone

replacement surgery such as hip and knee replacements.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 213250-70-5P 213319-29-0P

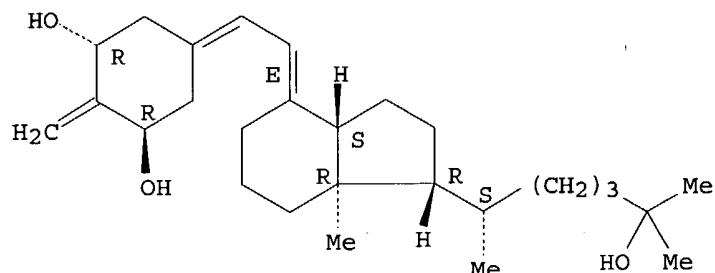
(preparation of 2-alkylnor-vitamin D compds. and their biol. activities)

RN 213250-70-5 USPTFULL

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E,20S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

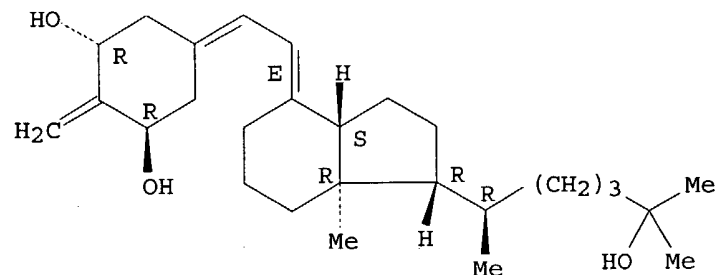


RN 213319-29-0 USPTFULL

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L33 ANSWER 3 OF 22 USPTFULL on STN

AN 2004:70585 USPTFULL

TI Method of extending the dose range of vitamin D compounds

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Pike, John W., Madison, WI, UNITED STATES

Shevde, Nirupama, Madison, WI, UNITED STATES

Plum, Lori A., Madison, WI, UNITED STATES

Clagett-Dame, Margaret, Deerfield, WI, UNITED STATES

PI US 2004053813 A1 20040318

AI US 2002-235244 A1 20020905 (10)

DT Utility

FS APPLICATION

LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE  
1100, MILWAUKEE, WI, 53202

CLMN Number of Claims: 68

ECL Exemplary Claim: 1

DRWN 2 Drawing Page(s)

LN.CNT 1122

CAS INDEXING IS AVAILABLE FOR THIS PATENT.



AB Inhibitors of bone calcium resorption are administered to allow high doses of vitamin D compounds or mimetics to be given with the intent of treating non-calcium related diseases such as cancer, psoriasis, and autoimmune disease without the dangers of calcification of kidney, heart, and aorta. Inhibitors of bone calcium resorption include the bis-phosphonates, OPG or the soluble RANKL receptor known as sRANK, and function to block the availability of calcium from bone thereby preventing hypercalcemia and the resulting calcification of soft tissues. Thus, high doses of  $1\alpha,25$ -dihydroxyvitamin D.sub.3 ( $1,25$ -(OH).sub.2D.sub.3), its analogs, prodrugs, or mimetics can be utilized with minimal risk to a patient. Specifically, alendronate is shown to block the bone calcium mobilization activity of both  $1,25$ -(OH).sub.2D.sub.3 and its very potent analog, 2-methylene-19-nor-(20S)- $1\alpha,25$ -dihydroxyvitamin D.sub.3.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 213319-29-0

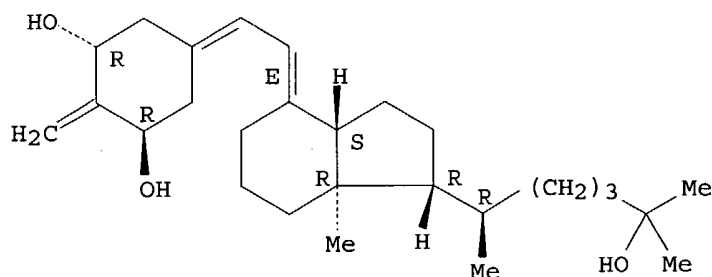
(method of extending dose range of vitamin D compds.)

RN 213319-29-0 USPATFULL

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
( $1\alpha,3\beta,7E$ )-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L33 ANSWER 4 OF 22 USPATFULL on STN

AN 2003:258374 USPATFULL

TI 26,27-homologated-20-EPI-2-alkylidene-19-nor-vitamin D compounds

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Sicinski, Rafal R., Warsaw, POLAND

PA Wisconsin Alumni Research Foundation, Madison, WI, UNITED STATES (U.S. corporation)

PI US 2003181427 A1 20030925

US 6696431 B2 20040224

AI US 2003-352745 A1 20030128 (10)

RLI Division of Ser. No. US 2001-1711, filed on 31 Oct 2001, GRANTED, Pat.

No. US 6537981 Division of Ser. No. US 2000-540686, filed on 31 Mar

2000, GRANTED, Pat. No. US 6392071 Continuation of Ser. No. US

1999-370966, filed on 10 Aug 1999, ABANDONED Continuation of Ser. No. US

1998-151113, filed on 10 Sep 1998, GRANTED, Pat. No. US 5936133 Division

of Ser. No. US 1997-819693, filed on 17 Mar 1997, GRANTED, Pat. No. US

5843928

DT Utility

FS APPLICATION

LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE  
1100, MILWAUKEE, WI, 53202

CLMN Number of Claims: 48

ECL Exemplary Claim: 1

DRWN 2 Drawing Page(s)

LN.CNT 1598

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides a novel class of vitamin D related compounds, namely, the 2-alkylidene-19-nor-vitamin D derivatives, as well as a general method for their chemical synthesis. The compounds have the formula: ##STR1##

where Y.sub.1 and Y.sub.2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 and R.sub.8, which may be the same or different, are each selected from hydrogen, alkyl, hydroxyalkyl and fluoroalkyl, or when taken together represent the group --(CH.sub.2).sub.x-- where x is an integer from 2 to 5, and where the group R represents any of the typical side chains known for vitamin D type compounds. These 2-substituted compounds are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 213250-70-5P

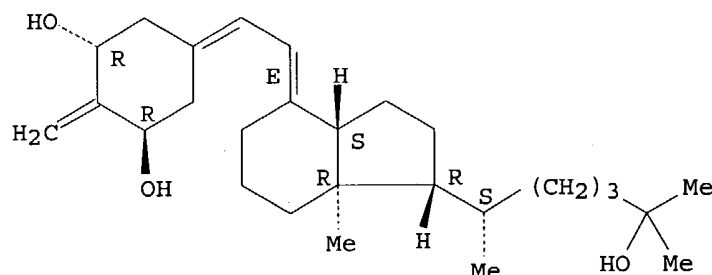
(preparation of 2-alkylidenenor-vitamin D compds.)

RN 213250-70-5 USPATFULL

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 $\alpha$ ,3 $\beta$ ,7E,20S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L33 ANSWER 5 OF 22 USPATFULL on STN

AN 2003:106944 USPATFULL

TI 26,27-Homologated-20-epi-2-alkyl-19-nor-vitamin D compounds

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Sicinski, Rafal R., Warsaw, POLAND

PI US 2003073857 A1 20030417

US 6667298 B2 20031223

AI US 2002-246968 A1 20020919 (10)

RLI Division of Ser. No. US 2001-999299, filed on 31 Oct 2001, PENDING

Division of Ser. No. US 2000-541470, filed on 31 Mar 2000, GRANTED, Pat.

No. US 6316642 Continuation-in-part of Ser. No. US 1999-454013, filed on

3 Dec 1999, GRANTED, Pat. No. US 6277837 Division of Ser. No. US

1998-135463, filed on 17 Aug 1998, GRANTED, Pat. No. US 6127559

Continuation-in-part of Ser. No. US 1997-819694, filed on 17 Mar 1997,

GRANTED, Pat. No. US 5945410

DT Utility

FS APPLICATION

LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE

1100, MILWAUKEE, WI, 53202

CLMN Number of Claims: 46

ECL Exemplary Claim: 1

DRWN 6 Drawing Page(s)

LN.CNT 2101

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides a novel class of vitamin D related compounds, namely, the 2-alkyl-19-nor-vitamin D derivatives, as well as a general method for their chemical synthesis. The compounds have the formula:  
##STR1##

where Y.sub.1 and Y.sub.2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 is selected from the group consisting of alkyl, hydroxyalkyl and fluoroalkyl, and where the group R represents any of the typical side chains known for vitamin D type compounds. These 2-substituted compounds, especially the 2 $\alpha$ -methyl and the 2 $\alpha$ -methyl-20S derivatives, are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 213250-70-5P 213319-29-0P

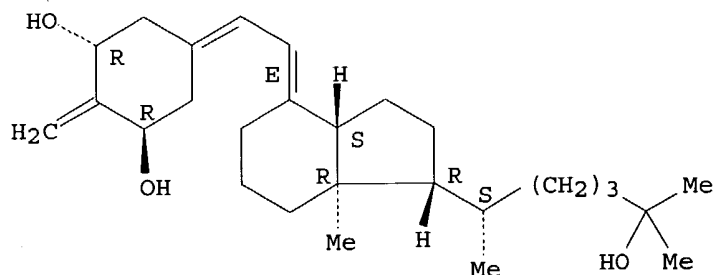
(preparation of 2-alkylnor-vitamin D compds. and their biol. activities)

RN 213250-70-5 USPATFULL

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

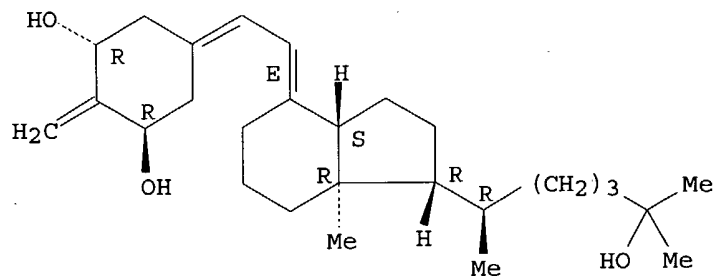


RN 213319-29-0 USPATFULL

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L33 ANSWER 6 OF 22 USPTAFULL on STN

AN 2002:273400 USPTAFULL

TI Use of 2α-methyl-19-nor-20(S)-1α,25-dihydroxyvitamin D3 to increase bone strength

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Smith, Connie M., Blue Mounds, WI, UNITED STATES

PI US 2002151528 A1 20021017

AI US 2001-45941 A1 20011019 (10)

RLI Division of Ser. No. US 2000-616778, filed on 14 Jul 2000, GRANTED, Pat. No. US 6306844 Continuation-in-part of Ser. No. US 1998-135463, filed on 17 Aug 1998, GRANTED, Pat. No. US 6127559 Continuation-in-part of Ser. No. US 1997-819694, filed on 17 Mar 1997, GRANTED, Pat. No. US 5945410

PRAI JP 2001-83085 20010322

DT Utility

FS APPLICATION

LREP Thomas M. Wozny, ANDRUS, SCEALES, STARKE & SAWALL, LLP, Suite 1100, 100 East Wisconsin Avenue, Milwaukee, WI, 53202-4178

CLMN Number of Claims: 29

ECL Exemplary Claim: 1

DRWN 3 Drawing Page(s)

LN.CNT 532

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides pharmaceutical uses for 2α-methyl-19-nor-20(S)-1α,25-dihydroxyvitamin D<sub>3</sub>. This compound is characterized by high bone calcium mobilization activity demonstrating preferential activity on bone. This results in a novel therapeutic agent for the treatment of diseases where bone formation is desired, particularly osteoporosis. This compound also exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocle thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis. This compound also increases both breaking strength and crushing strength of bones evidencing use in conjunction with bone replacement surgery such as hip and knee replacements.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 213250-70-5P 213319-29-0P

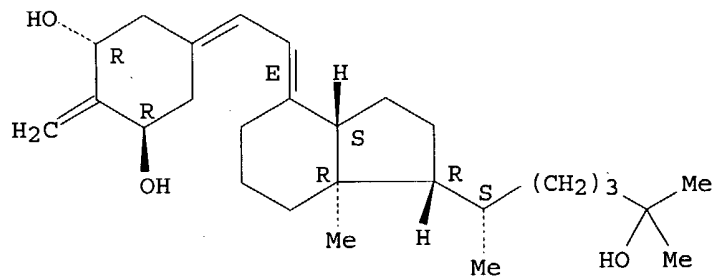
(preparation of 2-alkyl-nor-vitamin D compds. and their biol. activities)

RN 213250-70-5 USPTAFULL

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

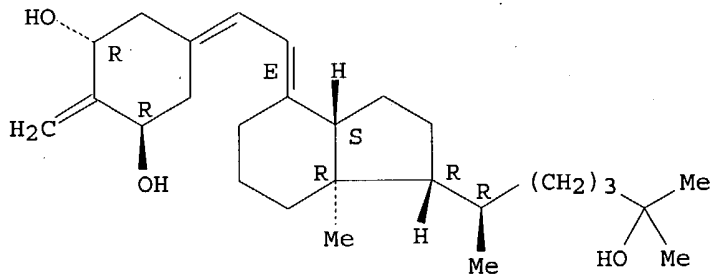
Absolute stereochemistry.

Double bond geometry as shown.



RN 213319-29-0 USPATFULL  
 CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
 (1 $\alpha$ ,3 $\beta$ ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



L33 ANSWER 7 OF 22 USPATFULL on STN  
 AN 2002:228475 USPATFULL  
 TI 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compounds  
 IN DeLuca, Hector F., Deerfield, WI, UNITED STATES  
 Sicinski, Rafal R., Warsaw, POLAND  
 PA Wisconsin Alumni Research Foundation, Madison, WI, UNITED STATES (U.S.  
 corporation)  
 PI US 2002123638 A1 20020905  
 US 6544969 B2 20030408  
 AI US 2001-999299 A1 20011031 (9)  
 RLI Division of Ser. No. US 2000-541470, filed on 31 Mar 2000, PATENTED  
 Continuation-in-part of Ser. No. US 1999-454013, filed on 3 Dec 1999,  
 PATENTED Division of Ser. No. US 1998-135463, filed on 17 Aug 1998,  
 PATENTED Continuation-in-part of Ser. No. US 1997-819694, filed on 17  
 Mar 1997, PATENTED  
 DT Utility  
 FS APPLICATION  
 LREP Thomas M. Wozny, ANDRUS, SCEALES, STARKE & SAWALL, LLP, Suite 1100, 100  
 East Wisconsin Avenue, Milwaukee, WI, 53202-4178  
 CLMN Number of Claims: 46  
 ECL Exemplary Claim: 1  
 DRWN 6 Drawing Page(s)  
 LN.CNT 2103  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 AB This invention provides a novel class of vitamin D related compounds,  
 namely, the 2-alkyl-19-nor-vitamin D derivatives, as well as a general  
 method for their chemical synthesis. The compounds have the formula:  
 ##STR1##

where Y.sub.1 and Y.sub.2, which may be the same or different, are each

selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 is selected from the group consisting of alkyl, hydroxyalkyl and fluoroalkyl, and where the group R represents any of the typical side chains known for vitamin D type compounds. These 2-substituted compounds, especially the 2 $\alpha$ -methyl and the 2 $\alpha$ -methyl-20S derivatives, are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 213250-70-5P 213319-29-0P

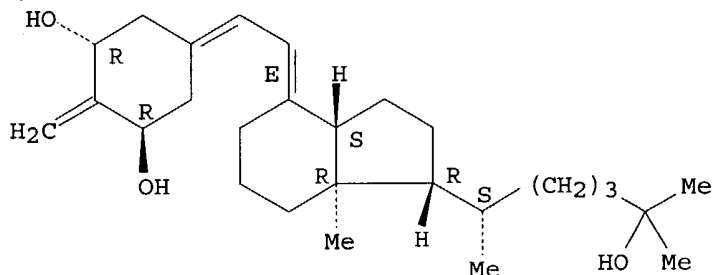
(preparation of 2-alkylnor-vitamin D compds. and their biol. activities)

RN 213250-70-5 USPATFULL

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E,20S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

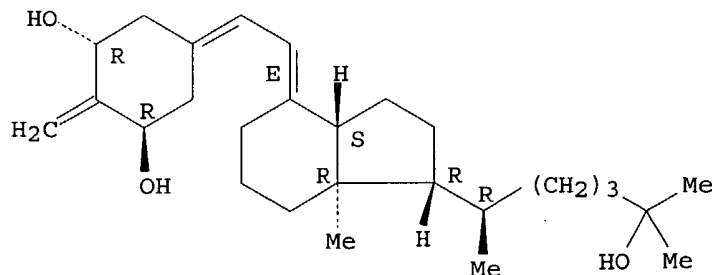


RN 213319-29-0 USPATFULL

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L33 ANSWER 8 OF 22 USPATFULL on STN

AN 2002:165381 USPATFULL

TI 26,27-homologated-20-EPI-2-alklidene-19-nor-vitamin D compounds

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Sicinski, Rafal R., Warsaw, POLAND

PA Wisconsin Alumni Research Foundation of Madison (U.S. corporation)

PI US 2002087015 A1 20020704

US 6537981 B2 20030325  
 AI US 2001-1711 A1 20011031 (10)  
 RLI Division of Ser. No. US 2000-540686, filed on 31 Mar 2000, PENDING  
 Continuation of Ser. No. US 1998-151113, filed on 10 Sep 1998, PATENTED  
 Division of Ser. No. US 1997-819693, filed on 17 Mar 1997, PATENTED  
 DT Utility  
 FS APPLICATION  
 LREP Thomas M. Wozny, ANDRUS, SCEALES, STARKE & SAWALL, LLP, Suite 1100, 100  
 East Wisconsin Avenue, Milwaukee, WI, 53202-4178  
 CLMN Number of Claims: 48  
 ECL Exemplary Claim: 1  
 DRWN 2 Drawing Page(s)  
 LN.CNT 1601

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides a novel class of vitamin D related compounds, namely, the 2-alkylidene-19-nor-vitamin D derivatives, as well as a general method for their chemical synthesis. The compounds have the formula: ##STR1##

where Y.sub.1 and Y.sub.2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 and R.sub.8, which may be the same or different, are each selected from hydrogen, alkyl, hydroxyalkyl and fluoroalkyl, or when taken together represent the group --(CH.sub.2).sub.X-- where x is an integer from 2 to 5, and where the group R represents any of the typical side chains known for vitamin D type compounds. These 2-substituted compounds are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

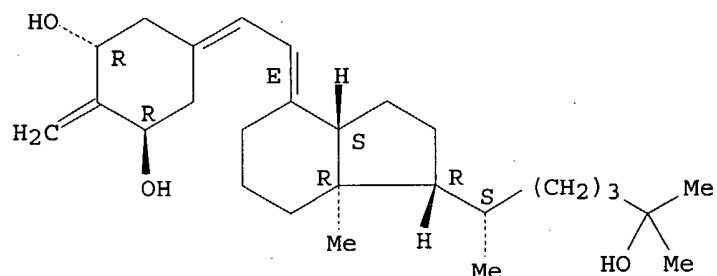
IT 213250-70-5P

(preparation of 2-alkylidenenor-vitamin D compds.)

RN 213250-70-5 USPATFULL

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
 (1 $\alpha$ ,3 $\beta$ ,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



L33 ANSWER 9 OF 22 USPATFULL on STN

AN 2002:116429 USPATFULL

TI 26,27-homologated-20-EPI-2-alkylidene-19-nor-vitamin D compounds

IN DeLuca, Hector F., Deerfield, WI, United States  
 Sicinski, Rafal R., Warsaw, POLAND

PA Wisconsin Alumni: Research Foundation, Madison, WI, United States (U.S. corporation)  
 PI US 6392071 B1 20020521  
 AI US 2000-540686 20000331 (9)  
 RLI Continuation-in-part of Ser. No. US 1999-370966, filed on 10 Aug 1999, now abandoned Continuation of Ser. No. US 1998-151113, filed on 10 Sep 1998, now patented, Pat. No. US 5936133 Division of Ser. No. US 1997-819693, filed on 17 Mar 1997, now patented, Pat. No. US 5843928  
 DT Utility  
 FS GRANTED  
 EXNAM Primary Examiner: Qazi, Sabiha  
 LREP Andrus, Sceales, Starke & Sawall, LLP  
 CLMN Number of Claims: 9  
 ECL Exemplary Claim: 1  
 DRWN 2 Drawing Figure(s); 2 Drawing Page(s)  
 LN.CNT 1372

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides a novel class of vitamin D related compounds, namely, the 2-alkylidene-19-nor-vitamin D derivatives, as well as a general method for their chemical synthesis. The compounds have the formula: ##STR1##

where Y.sub.1 and Y.sub.2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 and R.sub.8, which may be the same or different, are each selected from hydrogen, alkyl, hydroxyalkyl and fluoroalkyl, or when taken together represent the group --(CH.sub.2).sub.x-- where x is an integer from 2 to 5, and where the group R represents any of the typical side chains known for vitamin D type compounds. These 2-substituted compounds are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 213250-70-5P 213319-29-0P

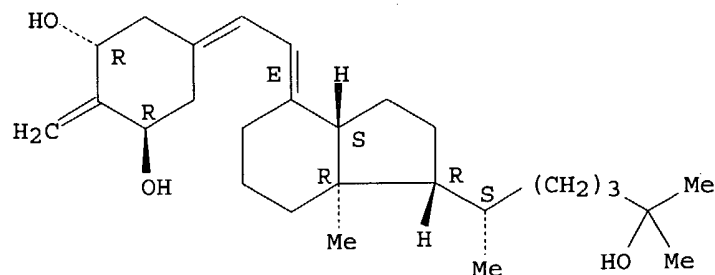
(preparation of 26,27-homologated-20-epi-2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

RN 213250-70-5 USPATFULL

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 $\alpha$ ,3 $\beta$ ,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



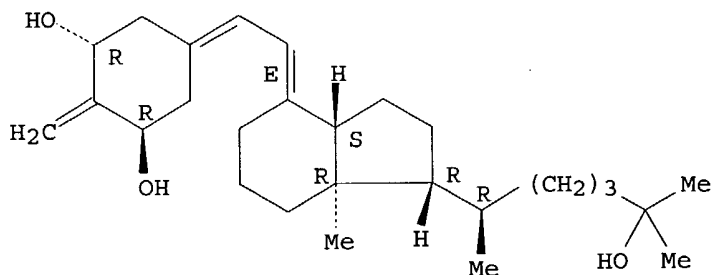
RN 213319-29-0 USPATFULL

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,



(1 $\alpha$ ,3 $\beta$ ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



L33 ANSWER 10 OF 22 USPATFULL on STN

AN 2002:99449 USPATFULL

TI 1alpha-hydroxy-2-methylene-19-nor-homopregnacalciferol and its uses

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES

Sicinski, Rafal R., Warsaw, POLAND

Gowlugari, Sumithra, Madison, WI, UNITED STATES

Plum, Lori A., Madison, WI, UNITED STATES

Clagett-Dame, Margaret, Deerfield, WI, UNITED STATES

PI US 2002052350 A1 20020502

US 6440953 B2 20020827

AI US 2001-878438 A1 20010611 (9)

RLI Continuation-in-part of Ser. No. US 2000-657828, filed on 8 Sep 2000,  
PENDING

DT Utility

FS APPLICATION

LREP Thomas M. Wozny, ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 East  
Wisconsin Avenue, Suite 1100, Milwaukee, WI, 53202-4178

CLMN Number of Claims: 33

ECL Exemplary Claim: 1

DRWN 7 Drawing Page(s)

LN.CNT 502

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses 1 $\alpha$ -hydroxy-2-methylene-19-nor-homopregnacalciferol and pharmaceutical uses therefor. This compound exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. This compound also has little, if any, calcemic activity and therefore may be used to treat immune disorders in humans as well as renal osteodystrophy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

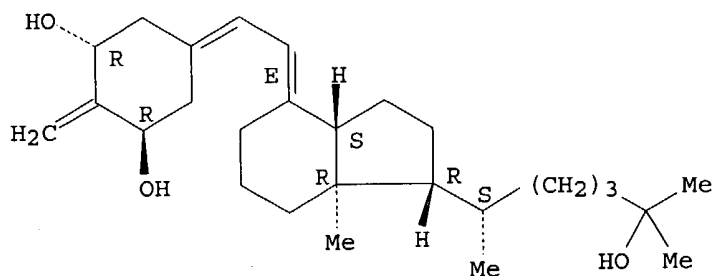
IT 213250-70-5

(hydroxymethylenenorhomopregnacalciferol and therapeutic use)

RN 213250-70-5 USPATFULL

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E,20S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



L33 ANSWER 11 OF 22 USPATFULL on STN

AN 2001:202815 USPATFULL

TI 26,27-Homologated-20-EPI-2alkyl-19-nor-vitamin D compounds

IN DeLuca, Hector F., Deerfield, WI, United States

Sicinski, Rafal R., Warsaw, Poland

PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)

PI US 6316642 B1 20011113

AI US 2000-541470 20000331 (9)

RLI Continuation-in-part of Ser. No. US 1999-454013, filed on 3 Dec 1999  
Division of Ser. No. US 1998-135463, filed on 17 Aug 1998, now patented,  
Pat. No. US 6127559 Continuation-in-part of Ser. No. US 1997-819694,  
filed on 17 Mar 1997, now patented, Pat. No. US 5945410

DT Utility

FS GRANTED

EXNAM Primary Examiner: Qazi, Sabiha

LREP Andrus, Sceales, Starke & Sawall, LLP

CLMN Number of Claims: 13

ECL Exemplary Claim: 1

DRWN 6 Drawing Figure(s); 6 Drawing Page(s)

LN.CNT 1931

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides a novel class of vitamin D related compounds, namely, 2-alkyl-19-nor-vitamin D derivatives, as well as a general method for their chemical synthesis. The compounds have the formula:  
##STR1##

where Y.sub.1 and Y.sub.2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 is selected from the group consisting of alkyl, hydroxyalkyl and fluoroalkyl, and where the group R represents any of the typical side chains known for vitamin D type compounds. These 2-substituted compounds, especially the 2 $\alpha$ -methyl and the 2 $\alpha$ -methyl-20S derivatives, are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

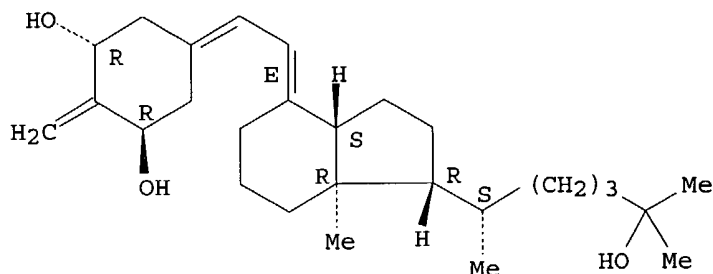
IT 213250-70-5P 213319-29-0P

(preparation of 26,27-homologated-20-epi-2-alkyl-19-norvitamin D compds. with high intestinal calcium transport activity)

RN 213250-70-5 USPATFULL

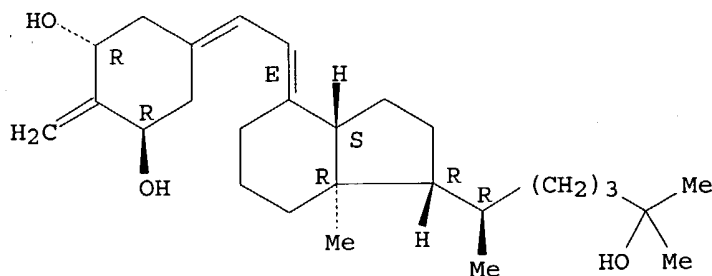
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E,20S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



RN 213319-29-0 USPATFULL  
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



L33 ANSWER 12 OF 22 USPATFULL on STN  
AN 2001:136640 USPATFULL  
TI 2-alkyl-19-nor-vitamin D compounds  
IN DeLuca, Jr., Hector F., Deerfield, WI, United States  
Sicinski, Rafal R., Warsaw, Poland  
PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S.  
corporation)  
PI US 6277837 B1 20010821  
AI US 1999-454013 19991203 (9)  
RLI Division of Ser. No. US 1998-135463, filed on 17 Aug 1998, now patented,  
Pat. No. US 6127559 Continuation-in-part of Ser. No. US 1997-819694,  
filed on 17 Mar 1997, now patented, Pat. No. US 5945410  
DT Utility  
FS GRANTED  
EXNAM Primary Examiner: Qazi, Sabiha  
LREP Andrus, Sceales, Starke & Sawall, LLP  
CLMN Number of Claims: 23  
ECL Exemplary Claim: 1  
DRWN 6 Drawing Figure(s); 6 Drawing Page(s)  
LN.CNT 1544  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AB This invention provides a novel class of vitamin D related compounds,  
namely, the 2-alkyl-19-nor-vitamin D derivatives, as well as a general  
method for their chemical synthesis. The compounds have the formula:  
##STR1##

where Y.sub.1 and Y.sub.2, which may be the same or different, are each

selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 is selected from the group consisting of alkyl, hydroxyalkyl and fluoroalkyl, and where the group R represents any of the typical side chains known for vitamin D type compounds. These 2-substituted compounds, especially the 2 $\alpha$ -methyl and the 2 $\alpha$ -methyl-20S derivatives, are characterized by relatively low intestinal calcium transport activity and high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 213250-70-5P 213319-29-0P

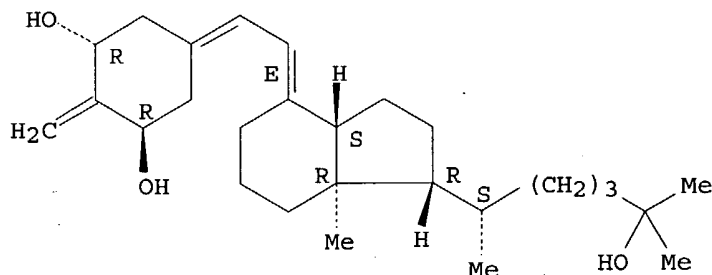
(preparation of 2-alkylnor-vitamin D compds. and their biol. activities)

RN 213250-70-5 USPTFULL

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E,20S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

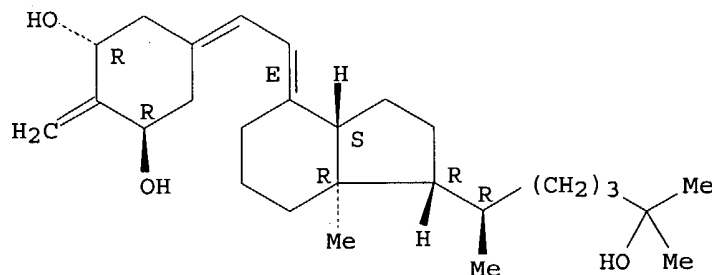


RN 213319-29-0 USPTFULL

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L33 ANSWER 13 OF 22 USPTFULL on STN

AN 2000:132031 USPTFULL

TI 2-alkyl-19-nor-vitamin D compounds

IN DeLuca, Hector F., Deerfield, WI, United States  
Sicinski, Rafal R., Warsaw, Poland

PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)

PI US 6127559 20001003  
 AI US 1998-135463 19980817 (9)  
 RLI Continuation-in-part of Ser. No. US 1997-819694, filed on 17 Mar 1997,  
 now patented, Pat. No. US 5945410  
 DT Utility  
 FS Granted  
 EXNAM Primary Examiner: Dees, Jose' G.; Assistant Examiner: Qazi, Sabiha N.  
 LREP Andrus, Sceales, Starke & Sawall  
 CLMN Number of Claims: 43  
 ECL Exemplary Claim: 1  
 DRWN 6 Drawing Figure(s); 6 Drawing Page(s)  
 LN.CNT 1575

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides a novel class of vitamin D related compounds, namely, the 2-alkyl-19-nor-vitamin D derivatives, as well as a general method for their chemical synthesis. The compounds have the formula: ##STR1## where Y.sub.1 and Y.sub.2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 is selected from the group consisting of alkyl, hydroxyalkyl and fluoroalkyl, and where the group R represents any of the typical side chains known for vitamin D type compounds. These 2-substituted compounds, especially the 2 $\alpha$ -methyl and the 2 $\alpha$ -methyl-20S derivatives, are characterized by relatively low intestinal calcium transport activity and high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

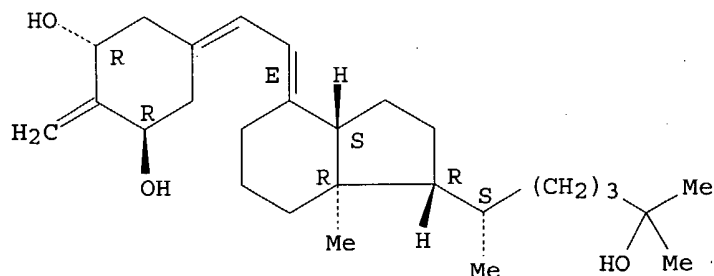
IT 213250-70-5P

(preparation and therapeutic use of 2-alkyl-19-nor-vitamin D analog)

RN 213250-70-5 USPATFULL

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
 (1 $\alpha$ ,3 $\beta$ ,7E,20S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



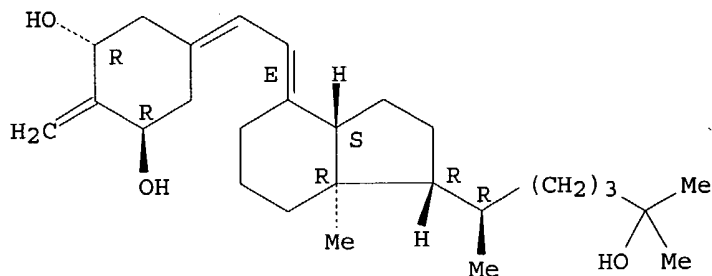
IT 213319-29-0P

(preparation and therapeutic use of 2-alkyl-19-nor-vitamin D analog)

RN 213319-29-0 USPATFULL

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
 (1 $\alpha$ ,3 $\beta$ ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



L33 ANSWER 14 OF 22 USPATFULL on STN

AN 1999:102799 USPATFULL

TI 2-alkyl-19-nor-vitamin D compounds

IN DeLuca, Hector F., Deerfield, WI, United States

Rafal, Sicinski R., Warsaw, Poland

PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)

PI US 5945410 19990831

AI US 1997-819694 19970317 (8)

DT Utility

FS Granted

EXNAM Primary Examiner: Dees, Jose' G.; Assistant Examiner: Pryor, Alton

LREP Andrus, Sceales, Starke & Sawall

CLMN Number of Claims: 41

ECL Exemplary Claim: 1

DRWN 2 Drawing Figure(s); 2 Drawing Page(s)

LN.CNT 1227

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides a novel class of vitamin D related compounds, namely, the 2-alkyl-19-nor-vitamin D derivatives, as well as a general method for their chemical synthesis. The compounds have the formula: ##STR1## where Y.sub.1 and Y.sub.2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 is selected from the group consisting of alkyl, hydroxyalkyl and fluoroalkyl, and where the group R represents any of the typical side chains known for vitamin D type compounds. These 2-substituted compounds are characterized by low intestinal calcium transport activity and high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 213250-70-5P 213319-29-0P

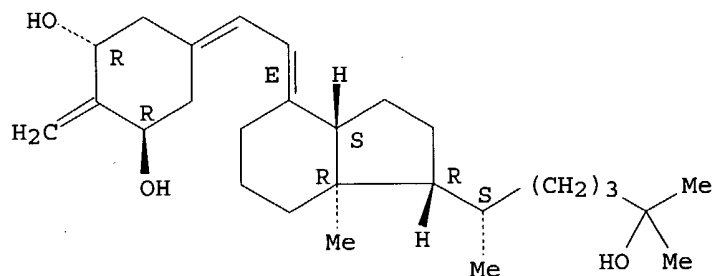
(preparation of 2-alkylnor-vitamin D compds. and their biol. activities)

RN 213250-70-5 USPATFULL

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 $\alpha$ ,3 $\beta$ ,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

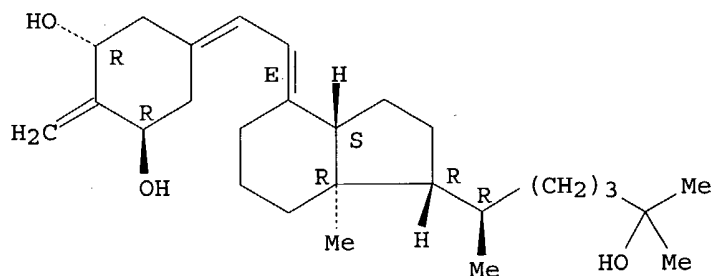
Double bond geometry as shown.



RN 213319-29-0 USPATFULL

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



L33 ANSWER 15 OF 22 USPATFULL on STN

AN 1999:92846 USPATFULL

TI 2-alkylidene-19-nor-vitamin D compounds

IN Deluca, Hector F., Deerfield, WI, United States

Sicinski, Rafal R., Warsaw, Poland

PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)

PI US 5936133 19990810

AI US 1998-151113 19980910 (9)

RLI Division of Ser. No. US 1997-819693; filed on 17 Mar 1997, now patented,  
Pat. No. US 5843928

DT Utility

FS Granted

EXNAM Primary Examiner: Lambkin, Deborah C.

LREP Andrus, Sceales, Starke & Sawall

CLMN Number of Claims: 12

ECL Exemplary Claim: 1

DRWN 2 Drawing Figure(s); 2 Drawing Page(s)

LN.CNT 1051

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides a novel class of vitamin D related compounds, namely, the 2-alkylidene-19-nor-vitamin D derivatives, as well as a general method for their chemical synthesis. The compounds have the formula: ##STR1## where Y.sub.1 and Y.sub.2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 and R.sub.8, which may be the same or different, are each selected from hydrogen, alkyl, hydroxyalkyl and fluoroalkyl, or when taken together represent the group --(CH.sub.2).sub.x-- where x is an integer from 2 to 5, and where the group R represents any of the typical side chains known for vitamin D

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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30-70-5F
(preparation of 2-alkylidenenor-vitamin D compds.)

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19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E,20S)- (9CI) (CA INDEX NAME)

AN 1999:92818 USPATFULL

IN Paaren, Herbert E., Madison, WI, United States

PA Tetrionics, Inc., Madison, WI, United States (U.S. corporation)

PI	US 5936105	19990810
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AI US 1998-96330 19980611 (9)

AI	US	1998-53099P	19970613	(60)
PRAI	US	1997-53088P	19970613	(60)

DT Utility

FS      Granted

EXNAM Primary Examiner: Clardy, S. Mark; Assistant Examiner: Pryor, Alton

LREP Ryndak &amp; Lyerla

CLMN Number of Claims: 1

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 919

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

19-nor-vitamin D analog compounds and a method of synthesizing such compounds are disclosed. More particularly, examples of such compounds include 14-epi-19-nor-1 $\alpha$ ,25-dihydroxyvitamin D.sub.3, 14-epi-20-epi-19-nor-1 $\alpha$ , 25-dihydroxyvitamin D.sub.3, 14-epi-20-epi-19-nor-1 $\alpha$ -hydroxyvitamin D.sub.3, 14-epi-19-nor-1 $\alpha$ , 25-dihydroxyvitamin D.sub.2, 14-epi-19-nor-24-homo-1 $\alpha$ , 25-dihydroxyvitamin D.sub.3, 14-epi-19-nor-20(S)-hydroxymethyl-1 $\alpha$ -hydropregnacalciferol, and 14-epi-19-nor-20(R)-hydroxymethyl-1 $\alpha$ -hydroxypregnacalciferol.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

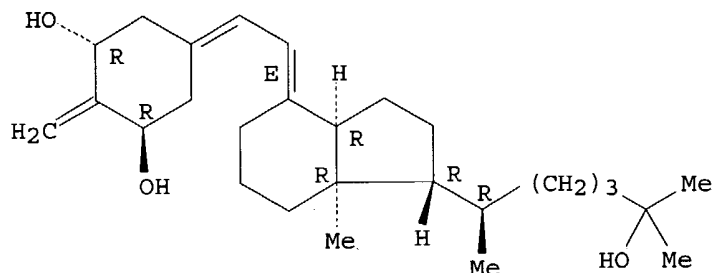
IT 235108-14-2P

08-14-2P  
(preparation of 14-epi-19-nor-vitamin D compds. with cell differentiation activity)



RN 235108-14-2 USPATFULL  
 CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
 (1 $\alpha$ ,3 $\beta$ ,7E,14 $\beta$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



L33 ANSWER 17 OF 22 USPATFULL on STN  
 AN 1998:150930 USPATFULL  
 TI 2-alkylidene-19-nor-vitamin D compounds  
 IN Deluca, Hector F., Deerfield, WI, United States  
 Rafal, Sicinski R., Warsaw, Poland  
 PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)  
 PI US 5843928 19981201  
 AI US 1997-819693 19970317 (8)  
 DT Utility  
 FS Granted  
 EXNAM Primary Examiner: Lambkin, Deborah C.  
 LREP Andrus, Sceales, Starke & Sawall  
 CLMN Number of Claims: 33  
 ECL Exemplary Claim: 1  
 DRWN 2 Drawing Figure(s); 2 Drawing Page(s)  
 LN.CNT 1153  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 AB This invention provides a novel class of vitamin D related compounds, namely, the 2-alkylidene-19-nor-vitamin D derivatives, as well as a general method for their chemical synthesis. The compounds have the formula: ##STR1## where Y.sub.1 and Y.sub.2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 and R.sub.8, which may be the same or different, are each selected from hydrogen, alkyl, hydroxyalkyl and fluoroalkyl, or when taken together represent the group --(CH.sub.2).sub.x-- where x is an integer from 2 to 5, and where the group R represents any of the typical side chains known for vitamin D type compounds. These 2-substituted compounds are characterized by low intestinal calcium transport activity and high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

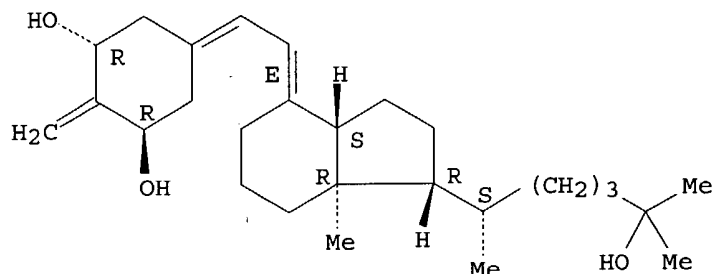
IT 213250-70-5P

(preparation of 2-alkylidenenor-vitamin D compds.)

RN 213250-70-5 USPATFULL

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
 (1 $\alpha$ ,3 $\beta$ ,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



L33 ANSWER 18 OF 22 USPAT2 on STN  
 AN 2003:258374 USPAT2  
 TI 26,27-homologated-20-EPI-2-alkylidene-19-nor-vitamin D compounds  
 IN DeLuca, Hector F., Deerfield, WI, United States  
 Sicinski, Rafal R., Warsaw, POLAND  
 PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)  
 PI US 6696431 B2 20040224  
 AI US 2003-352745 20030128 (10)  
 RLI Division of Ser. No. US 2001-1711, filed on 31 Oct 2001, now patented, Pat. No. US 6537981 Division of Ser. No. US 2000-540686, filed on 31 Mar 2000, now patented, Pat. No. US 6392071 Continuation of Ser. No. US 1999-370966, filed on 10 Aug 1999, now abandoned Continuation of Ser. No. US 1998-151113, filed on 10 Sep 1998, now patented, Pat. No. US 5936133 Division of Ser. No. US 1997-819693, filed on 17 Mar 1997, now patented, Pat. No. US 5843928  
 DT Utility  
 FS GRANTED  
 EXNAM Primary Examiner: Qazi, Sabiha  
 LREP Andrus, Sceales, Starke & Sawall, LLP  
 CLMN Number of Claims: 2  
 ECL Exemplary Claim: 1  
 DRWN 2 Drawing Figure(s); 2 Drawing Page(s)  
 LN.CNT 1382  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 AB This invention provides a novel class of vitamin D related compounds, namely, the 2-alkylidene-19-nor-vitamin D derivatives, as well as a general method for their chemical synthesis. The compounds have the formula: ##STR1##

where Y.sub.1 and Y.sub.2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 and R.sub.8, which may be the same or different, are each selected from hydrogen, alkyl, hydroxyalkyl and fluoroalkyl, or when taken together represent the group --(CH.sub.2).sub.x-- where x is an integer from 2 to 5, and where the group R represents any of the typical side chains known for vitamin D type compounds. These 2-substituted compounds are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 213250-70-5P

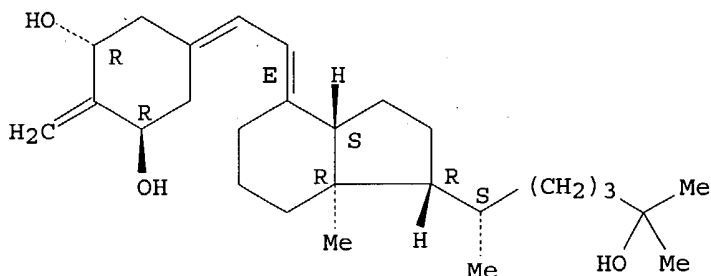
(preparation of 2-alkylidenenor-vitamin D compds.)

RN 213250-70-5 USPAT2

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L33 ANSWER 19 OF 22 USPAT2 on STN

AN 2003:106944 USPAT2

TI 26,27-Homologated-20-EPI-2-alkyl-19-NOR-vitamin D compounds

IN DeLuca, Hector F., Deerfield, WI, United States

Sicinski, Rafal R., Warsaw, POLAND

PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)

PI US 6667298 B2 20031223

AI US 2002-246968 20020919 (10)

RLI Division of Ser. No. US 2001-999299, filed on 31 Oct 2001, now patented, Pat. No. US 6544969, issued on 4 Aug 2000 Division of Ser. No. US 2000-541470, filed on 31 Mar 2000, now patented, Pat. No. US 6316642 Continuation-in-part of Ser. No. US 1999-454013, filed on 3 Dec 1999, now patented, Pat. No. US 6277837 Division of Ser. No. US 1998-135463, filed on 17 Aug 1998, now patented, Pat. No. US 6127559 Continuation-in-part of Ser. No. US 1997-819694, filed on 17 Mar 1997, now patented, Pat. No. US 5945410

DT Utility

FS GRANTED

EXNAM Primary Examiner: Qazi, Sabiha

LREP Andrus, Sceales, Starke & Sawall, LLP

CLMN Number of Claims: 20

ECL Exemplary Claim: 1

DRWN 6 Drawing Figure(s); 6 Drawing Page(s)

LN.CNT 1913

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides a novel class of vitamin D related compounds, namely, the 2-alkyl-19-nor-vitamin D derivatives, as well as a general method for their chemical synthesis. The compounds have the formula:  
##STR1##

where Y.sub.1 and Y.sub.2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 is selected from the group consisting of alkyl, hydroxyalkyl and fluoroalkyl, and where the group R represents any of the typical side chains known for vitamin D type compounds. These 2-substituted compounds, especially the 2 $\alpha$ -methyl and the 2 $\alpha$ -methyl-20S derivatives, are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the

treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

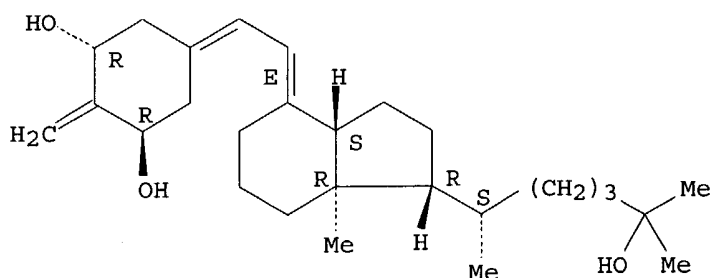
IT 213250-70-5P 213319-29-0P

(preparation of 2-alkylnor-vitamin D compds. and their biol. activities)

RN 213250-70-5 USPAT2

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E,20S)- (9CI) (CA INDEX NAME)

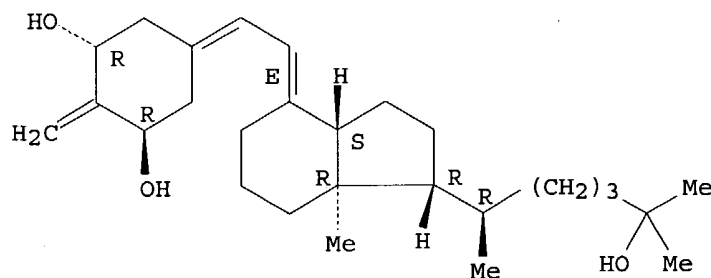
Absolute stereochemistry.  
Double bond geometry as shown.



RN 213319-29-0 USPAT2

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



L33 ANSWER 20 OF 22 USPAT2 on STN

AN 2002:228475 USPAT2

TI 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compounds

IN DeLuca, Hector F., Deerfield, WI, United States

Sicinski, Rafal R., Warsaw, POLAND

PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)

PI US 6544969 B2 20030408

AI US 2001-999299 20011031 (9)

RLI Division of Ser. No. US 2000-541470, filed on 31 Mar 2000, now patented, Pat. No. US 6316642 Continuation-in-part of Ser. No. US 1999-454013, filed on 3 Dec 1999, now patented, Pat. No. US 6277837 Division of Ser. No. US 1998-135463, filed on 17 Aug 1998, now patented, Pat. No. US 6127559 Continuation-in-part of Ser. No. US 1997-819694, filed on 17 Mar 1997, now patented, Pat. No. US 5945410

DT Utility  
 FS GRANTED  
 EXNAM Primary Examiner: Qazi, Sabiha  
 LREP Andrus, Sceales, Starke & Sawall, LLP  
 CLMN Number of Claims: 11  
 ECL Exemplary Claim: 1  
 DRWN 6 Drawing Figure(s); 6 Drawing Page(s)  
 LN.CNT 1884

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides a novel class of vitamin D related compounds, namely, the 2-alkyl-19-nor-vitamin D derivatives, as well as a general method for their chemical synthesis. The compounds have the formula:  
 ##STR1##

where Y.sub.1 and Y.sub.2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 is selected from the group consisting of alkyl, hydroxyalkyl and fluoroalkyl, and where the group R represents any of the typical side chains known for vitamin D type compounds. These 2-substituted compounds, especially the 2 $\alpha$ -methyl and the 2 $\alpha$ -methyl-20S derivatives, are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

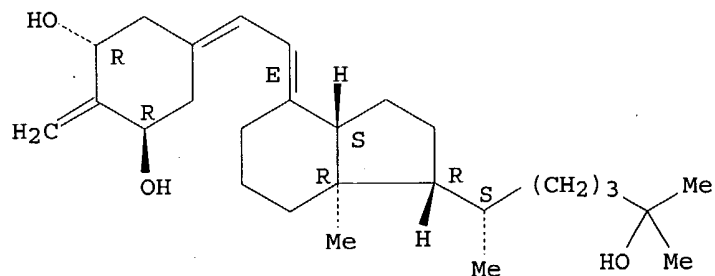
IT 213250-70-5P 213319-29-0P

(preparation of 2-alkylnor-vitamin D compds. and their biol. activities)

RN 213250-70-5 USPAT2

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
 (1 $\alpha$ ,3 $\beta$ ,7E,20S) - (9CI) (CA INDEX NAME)

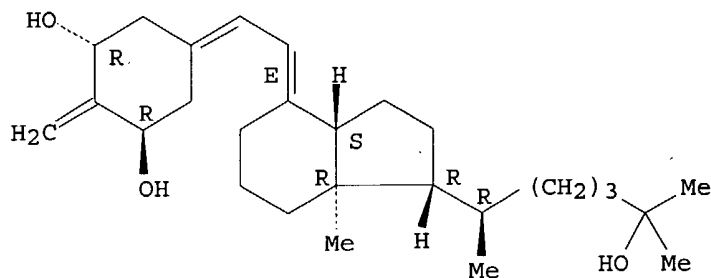
Absolute stereochemistry.  
 Double bond geometry as shown.



RN 213319-29-0 USPAT2

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
 (1 $\alpha$ ,3 $\beta$ ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



L33 ANSWER 21 OF 22 USPAT2 on STN  
 AN 2002:165381 USPAT2  
 TI 26,27-Homologated-20-EPI-2-alklidene-19-nor-vitamin D compounds  
 IN DeLuca, Hector F., Deerfield, WI, United States  
 Sicinski, Rafal R., Warsaw, POLAND  
 PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)  
 PI US 6537981 B2 20030325  
 AI US 2001-1711 20011031 (10)  
 RLI Division of Ser. No. US 2000-540686, filed on 31 Mar 2000 Continuation of Ser. No. US 1998-151113, filed on 10 Sep 1998, now patented, Pat. No. US 5936133 Division of Ser. No. US 1997-819693, filed on 17 Mar 1997, now patented, Pat. No. US 5843928  
 DT Utility  
 FS GRANTED  
 EXNAM Primary Examiner: Qazi, Sabiha  
 LREP Andrus, Sceales, Starke & Sawall, LLP  
 CLMN Number of Claims: 11  
 ECL Exemplary Claim: 1  
 DRWN 2 Drawing Figure(s); 2 Drawing Page(s)  
 LN.CNT 1385  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 AB This invention provides a novel class of vitamin D related compounds, namely, the 2-alkylidene-19-nor-vitamin D derivatives, as well as a general method for their chemical synthesis. The compounds have the formula: ##STR1##

where Y.sub.1 and Y.sub.2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 and R.sub.8, which may be the same or different, are each selected from hydrogen, alkyl, hydroxyalkyl and fluoroalkyl, or when taken together represent the group --(CH.sub.2).sub.X-- where x is an integer from 2 to 5, and where the group R represents any of the typical side chains known for vitamin D type compounds. These 2-substituted compounds are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

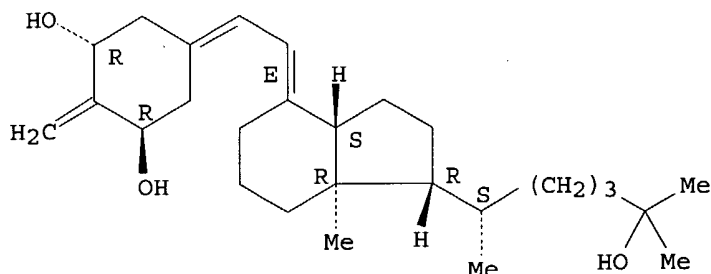
IT 213250-70-5P

(preparation of 2-alkylidenenor-vitamin D compds.)

RN 213250-70-5 USPAT2

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 $\alpha$ ,3 $\beta$ ,7E,20S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



L33 ANSWER 22 OF 22 USPAT2 on STN

AN 2002:99449 USPAT2

TI 1α-hydroxy-2-methylene-19-nor-homopregnacalciferol and its uses

IN DeLuca, Hector F., Deerfield, WI, United States

Sicinski, Rafal R., Warsaw, POLAND

Gowlugari, Sumithra, Madison, WI, United States

Plum, Lori A., Madison, WI, United States

Clagett-Dame, Margaret, Deerfield, WI, United States

PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)

PI US 6440953 B2 20020827

AI US 2001-878438 20010611 (9)

RLI Continuation-in-part of Ser. No. US 2000-657828, filed on 8 Sep 2000

DT Utility

FS GRANTED

EXNAM Primary Examiner: Qazi, Sabiha

LREP Andrus, Sceales, Starke & Sawall, LLP

CLMN Number of Claims: 26

ECL Exemplary Claim: 1

DRWN/ 7 Drawing Figure(s); 7 Drawing Page(s)

LN.CNT 485

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention discloses 1α-hydroxy-2-methylene-19-nor-homopregnacalciferol and pharmaceutical uses therefor. This compound exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anticancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. This compound also has little, if any, calcemic activity and therefore may be used to treat immune disorders in humans as well as renal osteodystrophy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

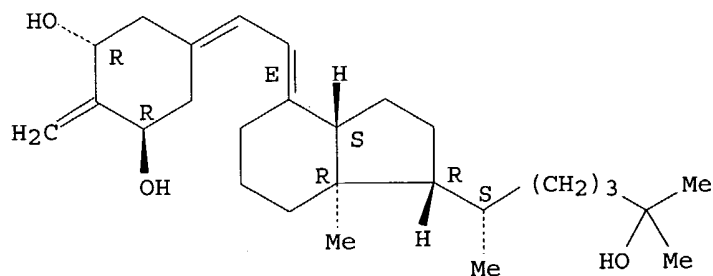
IT 213250-70-5

(hydroxymethylenenorhomopregnacalciferol and therapeutic use)

RN 213250-70-5 USPAT2

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



=> d his

(FILE 'HOME' ENTERED AT 13:40:41 ON 05 SEP 2004)  
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 13:41:00 ON 05 SEP 2004

E PLUM L/AU  
L1 22 S E3,E4,E6,E7  
E CLAGETTE M/AU  
L2 1 S E2  
E CLAGETTE D/AU  
E DAME M/AU  
L3 12 S E3,E4,E6-E8  
E DELUCA H/AU  
L4 1160 S E3,E6-E10  
E DE LUCA H/AU  
L5 38 S E5,E6  
L6 1213 S L1-L5

FILE 'REGISTRY' ENTERED AT 13:42:24 ON 05 SEP 2004

FILE 'HCAPLUS' ENTERED AT 13:42:24 ON 05 SEP 2004  
SET SMARTSELECT ON  
L7 SEL L6 1- RN : 2546 TERMS  
SET SMARTSELECT OFF

FILE 'REGISTRY' ENTERED AT 13:43:02 ON 05 SEP 2004

L8 2546 S L7  
L9 729 S L8 AND C6/ES AND C5-C6/ES AND 3/NR  
L10 294 S L9 AND 3/O  
L11 92 S L10 AND 27/C  
L12 54 S L11 AND 44/H  
L13 23 S L12 AND 1 3 25 TRIOL  
L14 2 S L13 AND 2 METHYLENE  
L15 52 S L12 NOT L14  
L16 STR  
L17 0 S L16 FAM SAM  
L18 3 S L16 FAM FUL  
SAV L18 QAZI782/A  
L19 3 S L14,L18

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L20 0 S L18

FILE 'HCAPLUS' ENTERED AT 13:48:23 ON 05 SEP 2004

L21 22 S L18  
L22 19 S L21 AND L6  
L23 3 S L21 NOT L22



L24 22 S L21-L23  
L25 0 S L24 AND LIFE(L) EXPECT?  
L26 0 S L24 AND LONGEV?  
E LONGEVITY/CT  
E E3+ALL  
L27 1 S L24 AND E3+OLD,NT,PFT,RT  
L28 22 S L24,L27

FILE 'USPATFULL, USPAT2' ENTERED AT 13:50:06 ON 05 SEP 2004  
L29 24 S L18

FILE 'REGISTRY' ENTERED AT 13:50:22 ON 05 SEP 2004

FILE 'HCAPLUS' ENTERED AT 13:50:36 ON 05 SEP 2004  
L30 21 S L28 NOT L27

FILE 'USPATFULL, USPAT2' ENTERED AT 13:51:17 ON 05 SEP 2004  
L31 0 S L29 AND LIFE(L) EXPECT?  
L32 2 S L29 AND (AGING? OR AGEING? OR LONGEV?)/CT,BI  
L33 22 S L29 NOT L32

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